# Assessment of the Scope and Quality of Clinical Practice Guidelines in Lung Cancer*

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***Study objectives:*** **To provide an evidence-based background for developing the American College of Chest Physicians (ACCP) lung cancer guidelines, a systematic review of the literature was performed to identify published lung cancer guidelines and evaluate their quality.**
***Design, setting, and participants:*** **A systematic search was performed for relevant literature from MEDLINE, Cancerlit, CINAHL, HealthStar, the Cochrane Library, and the National Guidelines Clearinghouse published from January 1989 to July 2001.**
***Measurement and results:*** **From 369 citations, 51 relevant guidelines were identified. Each guideline was evaluated by at least four reviewers using the Appraisal of Guidelines for Research and Evaluation (AGREE) instrument and was coded for clinical topics covered. The recommendations included in each guideline also were abstracted. Of the 51 guidelines evaluated, 27 (53%) were evidence-based. Clinical topics identified by the ACCP for their guideline effort each were represented by at least one existing guideline. Of the 880 clinical recommendations abstracted from the guidelines, only 253 (29%) were evidence-based. The AGREE instrument rates guidelines along six domains. As a group, the guidelines performed well in the scope and purpose domain, with only six guidelines (12%) scoring < 50%. For the remaining domains, however, the guidelines did not perform as well, as follows: for stakeholder involvement, 41 guidelines (80%) scored < 50%; for rigor of development, 29 guidelines (57%) scored < 50%; for clarity and presentation, 17 guidelines (33%) scored < 50%; for applicability, 46 guidelines (90%) scored < 50%; and for editorial independence, 47 guidelines (92%) scored < 50%. After considering the domain scores, the reviewers recommended only 19 of the guidelines (37%).**
***Conclusions:*** **All major clinical lung cancer topics are covered by at least one guideline, but no single guideline addresses all areas. Furthermore, although existing guidelines may accurately reflect clinical practice, most performed poorly when evaluated for quality. Future guideline efforts that address each item of the AGREE instrument would add substantially to the literature.**
***(CHEST 2003; 123:7S–20S)***

**Key words:** evidence-based medicine; lung neoplasms; practice guidelines

**Abbreviation:** AGREE = Appraisal of Guidelines for Research and Education

Lung cancer is the leading cause of cancer death for both men and women in the United States. In 2001, an estimated 169,500 new cases of lung cancer will have been diagnosed, and an estimated 157,400 deaths will have been attributed to the disease.[1] Current 5-year lung cancer survival rates are estimated at 14%.[1] Clinical practice guidelines are thought to be capable of improving quality, appropriateness, and cost-effectiveness of care.[2] A potential mechanism for improving outcomes in patients with lung cancer, then, would be to ensure that those patients are receiving evidence-based guideline care.

Clinical practice guidelines have been defined as "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."[2] However, the recent increase in the production of clinical practice guidelines has been accompanied by growing concern about the variations in guideline recommendations[3,4] and quality.[5–7]

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In 2001, a multidisciplinary panel was convened by the American College of Chest Physicians to develop evidence-based clinical practice guidelines for lung cancer diagnosis and treatment. To avoid potential duplication of effort, the first step taken was to identify and determine the quality of already published guidelines in this area.

## Materials and Methods

### *Identification of Guidelines*

Relevant guidelines were identified through computerized searches of MEDLINE, Cancerlit, CINAHL, HealthStar, the Cochrane Library, and the National Guidelines Clearinghouse, by reviewing the reference lists of review articles and included guidelines, and by consulting experts in the field. The search strategy used the MeSH terms *lung neoplasms* (exploded) and *bronchial neoplasms*, and required further indexing with publication type *guideline* or *practice guideline*, MeSH heading *guidelines*, or textword *guideline* or *guidelines*. Investigators reviewed English-language studies that had been published since 1989. Identified citations were screened for inclusion based on the following Institute of Medicine[2] definition of a guideline: "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances." Single-author overviews, secondary publications of practice guidelines, editorials, and letters to the editor were specifically excluded.

### *Appraisal Instrument*

The methodological quality of existing clinical practice guidelines was evaluated using the Appraisal of Guidelines for Research and Education (AGREE) instrument,[8] an international, rigorously developed, and validated instrument that compares well with other instruments designed for this purpose.[9] This instrument allowed for the assessment of several components that are integral to guideline development, as follows: (1) scope and purpose; (2) stakeholder involvement; (3) rigor of development; (4) clarity and presentation; (5) applicability; and (6) editorial independence. Five reviewers (LH, DM, ET, MK, and GS) used the AGREE instrument to evaluate the scientific quality of the lung cancer guidelines. A minimum of four reviewers completed the AGREE instrument for each guideline and also determined whether the guideline was evidence-based or consensus-based.

Each guideline was coded for the following topics covered: prevention; screening and early detection; initial evaluation; diagnosis; clinical staging; pathologic/surgical staging; treatment-early stage; treatment-stage I; treatment-stage II; treatment-stage IIIA/potentially resectable; treatment-stage IIIB/nonresectable; treatment-stage IV; treatment-Pancoast tumor, T4, and those requiring special consideration; treatment-small cell lung cancer; treatment-solitary pulmonary nodule; follow-up/surveillance; palliative care; palliative treatment; and practice organization.

The text of the recommendations included in each guideline also was abstracted. Each recommendation was coded for topic, subtopic, and type of evidence utilized when formulating the statement (*ie*, A, strong evidence; B, weak evidence; and C, consensus). Since different guidelines used different scales to rate the strength and quality of evidence supporting a particular recommendation, we often had to map published grades to our scale. In general, statements were graded as strong evidence (A) if they were supported by randomized controlled trials, weak evidence (B) if they were supported by evidence other than that from randomized controlled trials, and consensus (C) if they were not supported by clear study data. For guidelines that did not grade recommendations, we categorized statements based on the above schema.

### *Evaluation of Guidelines*

The 23-item AGREE instrument is divided into the following six domains (see "Appendix"): scope and purpose (three items); stakeholder involvement (four items); rigor of development (seven items); clarity and presentation (four items); applicability (three items); and editorial independence (two items). The score for each domain is obtained by summing up all the scores of the individual items in a domain and then standardizing as follows:

$$\frac{\text{obtained score - minimum possible score}}{\text{maximum possible score - minimum possible score}}$$

The maximum score for each domain would be the number of questions multiplied by the number of reviewers multiplied times 4 (*ie*, the score for strongly agree). The minimum possible score for a domain would be the number of questions multiplied times the number of reviewers multiplied times 1 (*ie*, the score for strongly disagree).

The final component of the AGREE instrument involves a recommendation regarding the use of the guidelines in practice as "strongly recommended," "recommended (with provisos or alterations)," "would not recommend," or "unsure." On this item, the investigators reached consensus for each guideline. For ease of interpretation, we considered "strongly recommended" and "recommended with provisos or alterations" as a response of "recommended," and "would not recommend" or "unsure" as a response of "would not recommend." The AGREE instrument instructs the raters to make a judgment as to the quality of the guideline, taking each of the appraisal criteria into consideration. In our ratings, we took into account the date of the guideline and considered whether we would recommend the document as a useful tool that could be adapted locally by a health-care provider who was considering implementing the guideline in a health-care practice or system. We placed relatively more weight on the quality of development than on whether the recommendations matched our particular clinical practice or were feasible in our particular practice environments.

Prior to evaluating the guidelines included in the review, we first each rated a superseded guideline,[10] compared ratings among reviewers, discussed discrepancies, and reached consensus about the interpretation of each question.

We used the $\kappa$ statistic as a measure of the agreement among reviewers.[11] However, before performing any calculations, the response categories were dichotomized into strongly agree/agree vs strongly disagree/disagree, as we thought that an analysis of agreement at this level was sufficient. The $\kappa$ statistic was then applied to each of the 23 items of the AGREE instrument. The simple proportion of agreement also was calculated.

## Results

We screened 308 citations that had been identified through computerized and other database searches, and an additional 61 citations that had been identified through clinical experts, reference lists, web site searches, and other sources. A total of 81 candidate

guidelines were selected, and, after reviewing the full text of each reference relative to the Institute of Medicine definition for a clinical practice guideline, a total of 51 guidelines were selected for this review (Table 1).[12–62]

Of the 51 guidelines, 47% were consensus-based, and the remaining 53% were evidence-based. Except for two guidelines, all had been written in the past 5 years. All clinical topics defined by the American College of Chest Physicians were represented by at least one guideline, with a range of 8 to 118 recommendations per topic (Table 2). Some recommendations were pertinent to more than one clinical topic. When this occurred, the recommendation was referenced to all relevant topics. A significant degree of overlap occurred across the clinical topics. This is illustrated by the category "solitary pulmonary nodule." Recommendations that specifically discussed the solitary pulmonary nodule were categorized under this topic; however, some recommendations under the topics "clinical staging," "diagnosis," and "small cell lung cancer" also were relevant to the "solitary pulmonary nodule" category.

Of the total of 880 clinical recommendations, the majority (71%) were consensus-based. There was a notable dearth of evidence-based recommendations for the following: diagnosis; initial evaluation and preparation; follow-up/surveillance; treatment of the solitary pulmonary nodule, early stage, and special cases (*eg*, Pancoast tumor, T4); and palliative care and treatment.

The quality of the guidelines is represented by the AGREE domain scores in Table 3.

### *AGREE Results*

*Scope and Purpose:* The score for this domain represents the degree to which the overall objectives of the guideline, the clinical questions covered, and the patients to whom the guideline was meant to apply were specifically described. Overall, the mean score was 72% (range, 29 to 97%), indicating that, on average, 72% of the criteria for scope and purpose were met. Most guidelines performed well in this domain, with only six guidelines (12%) scoring $< 50\%$.

*Stakeholder Involvement:* This domain evaluates the degree to which the guideline represents the views of its intended users. Included are questions regarding the composition of the guideline development group (specifically, whether individuals from all relevant professional groups were represented), whether patients' experiences and expectations informed the development of the guideline, whether the target users of the guideline were well-defined, and whether the guideline was piloted among end-users. Overall, the mean score for this domain was 35% (range, 3 to 70%), with 41 guidelines (80%) scoring $< 50\%$. Only 6% of guidelines included individuals from all relevant professional groups in the development stage, and none was piloted among end-users.

*Rigor of Development:* This domain specifically evaluates whether systematic methods were used to search for evidence, whether the criteria for selecting the evidence and the methods used to formulate the recommendations were clearly described, whether there was an explicit link between the recommendations and the supporting evidence, whether health benefits, side effects, and risks were considered when formulating the recommendations, whether the guideline was externally reviewed by experts prior to publication, and whether a procedure for updating the guideline was provided. Overall, the mean score for this domain was 52% (range, 2 to 95%), with 57% of guidelines scoring $< 50\%$. Specifically, only 16 guidelines (31%) described systematic methods for searching and selecting the evidence, 18 guidelines (35%) considered health benefits, side effects, and risks when formulating the recommendations, and 20 guidelines (39%) described the methods used to formulate the recommendations. Moreover, only 18 guidelines (35%) were externally reviewed prior to publication.

*Clarity and Presentation:* This domain describes the clarity of the guidelines. Specifically, it describes whether the recommendations were specific and unambiguous, whether the different management options were clearly presented, whether key recommendations were easily identifiable, and whether the guideline was supported with tools for application. Overall, the mean score for this domain was 57% (range, 15 to 90%). Only two guidelines (4%) included tools for application. Seventeen guidelines (33%) scored $< 50\%$ for this domain.

*Applicability:* This domain evaluates issues that are pertinent to guideline implementation. More specifically, it considers organizational barriers, cost implications, and monitoring criteria. The score on this domain was the lowest of all, with a mean score of 20% (range, 0 to 98%). Only five guidelines (10%) scored at least 50%. Two guidelines provided review criteria for monitoring purposes, and six discussed potential organizational barriers. No guideline discussed cost implications.

*Editorial Independence:* This domain addresses

**Table 1—*Lung Cancer Clinical Practice Guidelines**

| Authors | Date | Title | Evidence-Based or Consensus-Based? | Topics Covered |
|---|---|---|---|---|
| AATS, STS, STSA, and WTSA | 1993 | Practice guidelines in cardiothoracic surgery[12] | Consensus-based | Treatment-special case |
| ACS | 2001 | ACS guidelines for the early detection of cancer: update of early detection guidelines for prostate, colorectal, and endometrial cancers; also update 2001—testing for early lung cancer detection[13] | Consensus-based | Screening and early detection |
| ACR | 2000 | ACR appropriateness criteria: nonaggressive, nonsurgical treatment of inoperable NSCLC[14] | Consensus-based | Treatment-stages I, IIIA, IIIB, IV |
| ACR | 2000 | ACR appropriateness criteria: non-small cell lung cancer, nonsurgical, aggressive therapy[15] | Consensus-based | Treatment-stages IIIb, IV |
| ACR | 2000 | ACR appropriateness criteria: work-up of the solitary pulmonary nodule[16] | Consensus-based | Treatment-solitary pulmonary nodule |
| ACR | 1999 | ACR appropriateness criteria: follow-up and retreatment of brain metastases[17] | Consensus-based | Treatment-stage IV |
| ACR | 1999 | ACR appropriateness criteria: follow-up of non-small cell lung cancer[18] | Consensus-based | Follow-up/surveillance |
| ACR | 1999 | ACR appropriateness criteria: multiple brain metastases[19] | Consensus-based | Treatment-stage IV |
| ACR | 1999 | ACR appropriateness criteria: neoadjuvant therapy for marginally respectable (clinical N2) non-small cell lung cancer[20] | Consensus-based | Treatment-stage IIIA |
| ACR | 1999 | ACR appropriateness criteria: postoperative radiotherapy in non-small cell lung cancer[21] | Consensus-based | Treatment-stages I, II, IIIA |
| ACR | 1999 | ACR appropriateness criteria: preirradiation evaluation and management of brain metastases[22] | Consensus-based | Treatment-stage IV |
| ACR | 1999 | ACR appropriateness criteria: solitary brain metastasis[23] | Consensus-based | Treatment-small cell lung cancer, stage IV |
| ACR | 1999 | ACR appropriateness criteria: staging of bronchogenic carcinoma, non-small cell lung carcinoma[24] | Consensus-based | Clinical staging |
| ACR | 1999 | ACR appropriateness criteria: staging of non-small cell lung carcinoma[25] | Consensus-based | Clinical staging |
| AES, Clinical Research Committee | 1993 | Consensus guidelines for high dose rate remote brachytherapy in cervical, endometrial, and endobronchial tumors[26] | Consensus-based | Palliative treatment |
| ASCO | 1997 | Clinical practice guidelines for the treatment of unresectable non-small cell lung cancer[27] | Evidence-based | Clinical staging; diagnosis; follow-up/surveillance; pathologic/surgical staging, prevention; treatment-stages IIIb, IV |
| ATS | 2000 | Management of malignant pleural effusions[28] | Consensus-based | Palliative treatment; treatment-stage IV |
| ATS | 1989 | Guidelines for percutaneous transthoracic needle biopsy[29] | Consensus-based | Diagnosis; treatment-solitary pulmonary nodule |
| ATS and ERS | 1997 | Pretreatment evaluation of non-small cell lung cancer[30] | Consensus-based | Clinical staging; diagnosis; initial evaluation/preparation; screening and early detection |

**Table 1—*Continued**

| Authors | Date | Title | Evidence-Based or Consensus-Based? | Topics Covered |
|---|---|---|---|---|
| ACCC | 2000 | Oncology patient management guidelines: small cell lung cancer[31] | Consensus-based | Clinical staging; diagnosis; follow-up/surveillance; initial evaluation/preparation; pathologic/surgical staging; treatment-small cell lung cancer; stages I, II, IIIA, IIIB, and IV |
| Biesalski et al | 1997 | Consensus statement on lung cancer[32] | Consensus-based | Prevention |
| BTS and SCSGBI Working Party | 2001 | BTS guidelines: guidelines on the selection of patients with lung cancer for surgery[33] | Evidence-based | Clinical staging; follow-up/surveillance; initial evaluation/preparation; pathologic/surgical staging; practice organization; treatment-small cell lung cancer, Pancoast tumor, and stages I, II, IIIA, IIIB, and IV |
| BTS Standards of Care Committee Lung Cancer Working Party | 1998 | BTS recommendations to respiratory physicians for organizing the care of patients with lung cancer[34] | Evidence-based | Clinical staging; diagnosis; follow-up/surveillance; initial evaluation/preparation; palliative care; practice organization; screening and early detection; treatment-small cell lung cancer, Pancoast, tumor and stages I, II, IIIA, IIIB, and IV |
| CCOPGI | 2001 | The role of combination chemotherapy in the initial management of limited-stage small cell lung cancer[35] | Evidence-based | Treatment-small cell lung cancer |
| CCOPGI | 2001 | The role of single-agent docetaxel† as a second-line treatment for advanced non-small cell lung cancer[36] | Evidence-based | Treatment-stage IV |
| CCOPGI | 2000 | Altered fractionation of radical radiation therapy in the management of unresected non-small cell lung cancer[37] | Evidence-based | Treatment-stage IIIB |
| CCOPGI | 2000 | Chemotherapy in stage IV (metastatic) non-small cell lung cancer[38] | Evidence-based | Treatment-stage IV |
| CCOPGI | 2000 | Postoperative adjuvant chemotherapy and/or radiation therapy in stage II or IIIA completely resected non-small cell lung cancer[39] | Evidence-based | Treatment-stages II, IIIA |
| CCOPGI | 2000 | Prophylactic cranial irradiation in small cell lung cancer[40] | Evidence-based | Treatment-small cell lung cancer |
| CCOPGI | 2000 | The role of thoracic radiotherapy as an adjunct to standard chemotherapy in limited-stage small cell lung cancer[41] | Evidence-based | Treatment-small cell lung cancer |
| CCOPGI | 2000 | Unresected stage III non-small cell lung cancer[42] | Evidence-based | Treatment-stage IIIB |
| CCOPGI | 2000 | Use of gemcitabine in non-small cell lung cancer[43] | Evidence-based | Treatment-stages IIIB, IV |
| CCOPGI | 2000 | Use of preoperative chemotherapy with or without postoperative radiotherapy in technically resectable stage IIIA non-small cell lung cancer[44] | Evidence-based | Treatment-stage IIIA |
| CCOPGI | 2000 | Use of vinorelbine in non-small cell lung cancer[45] | Evidence-based | Treatment-stages IIIB, IV |

**Table 1—*Continued**

| Authors | Date | Title | Evidence-Based or Consensus-Based? | Topics Covered |
|---|---|---|---|---|
| CGG | 1998 | Guidance on commissioning cancer services: improving outcomes in lung cancer; the manual[46] | Evidence-based | Clinical staging; diagnosis; palliative care and treatment; pathologic/surgical staging; practice organization; prevention; screening and early detection; treatment-small cell lung cancer, stages I, II, IIIA, IIIB, and IV |
| Collège des Médecins du Québec | 1999 | Clinical practice guidelines: smoking prevention and cessation[47] | Evidence-based | Prevention |
| ESMO | 2001 | ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of non-small-cell lung cancer[48] | Evidence-based | Palliative care; treatment-stages I, II |
| ESMO | 2001 | ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of small-cell lung cancer[49] | Evidence-based | Treatment-small cell lung cancer |
| HCHP Adult Screening and Prevention Task Force | 1989 | Screening for lung cancer[50] | Evidence-based | Screening and early detection |
| NCI | 2001 | Lung cancer (PDQ): prevention[51] | Evidence-based | Prevention |
| NCI | 2001 | Lung cancer (PDQ): screening[52] | Evidence-based | Screening and early detection |
| NCI | 2001 | Non-small cell lung cancer (PDQ): treatment[53] | Evidence-based | Clinical staging; diagnosis; follow-up/ surveillance; initial evaluation/ preparation; pathologic/surgical staging; treatment-Pancoast tumor and stages I, II, IIIA, IIIB, and IV |
| NCI | 2000 | Small cell lung cancer (PDQ): treatment[54] | Evidence-based | Treatment-small cell lung cancer |
| NCCN | 2000 | NCCN practice guidelines for non-small cell lung cancer[55] | Consensus-based | Clinical staging; follow-up/surveillance; pathologic/surgical staging; treatment-stages IIIB, IV |
| NCCN | 2000 | NCCN practice guidelines for small cell lung cancer[56] | Consensus-based | Clinical staging; follow-up/surveillance; initial evaluation/preparation; treatment-small cell lung cancer |
| RCR Clinical Oncology Information Network | 1999 | Guidelines on the nonsurgical management of lung cancer[57] | Evidence-based | Practice organization; treatment-small cell lung cancer, stage IIIB |
| Scottish Intercollegiate Guidelines Network | 1998 | Management of lung cancer: a national clinical guideline recommended for use in Scotland[58] | Evidence-based | Clinical staging; diagnosis; palliative care; palliative treatment; pathological/surgical staging; practice organization; treatment-small cell lung cancer, early stage, Pancoast tumor, and stages I, II, IIIA, IIIB, and IV |
| SSO | 1997 | Lung cancer surgical practice guidelines[59] | Consensus-based | Clinical staging; diagnosis; initial evaluation/preparation; palliative treatment; pathologic/surgical staging; practice organization; screening and early detection; treatment-small cell lung cancer, stages I, II, IIIA, IIIB, IV |
| Timothy et al | 1990 | Workshop on consensus guidelines for management of lung cancer[60] | Consensus-based | Clinical staging; diagnosis; pathological/ surgical staging |
| US DHHS | 2000 | Treating tobacco use and dependence[61] | Evidence-based | Prevention |
| US Preventive Services Task Force | 1996 | Screening for lung cancer[62] | Evidence-based | Prevention; screening and early detection |

*ACR = American College of Radiology; BTS = British Thoracic Society; CCOPGI = Cancer Care Ontario Practice Guidelines Initiative; ESMO = European Society for Medical Oncology; NCCN = National Comprehensive Cancer Network; ACS = American Cancer Society; ASCO = American Society of Clinical Oncology; ATS = American Thoracic Society; NCI = National Cancer Institute; AATS = American Association for Thoracic Surgery; STS = Society of Thoracic Surgeons; STSA = Southern Thoracic Surgical Association; WTSA = Western Thoracic Surgical Association; AES = American Endocurietherapy Society; ACCC = Association of Community Cancer Centers; SCSGBI = Society of Cardiothoracic Surgeons of Great Britain and Ireland; HCHP = Harvard Community Health Plan; RCR = Royal College of Radiologists; SSO = Society of Surgical Oncology; DHHSI = Department of Health and Human Services; ERS = European Respiratory Society; CGG = Cancer Guidance Group.
†Taxotere; Aventis Pharmaceuticals; Bridgewater, NJ.

**Table 2—*Number of Guidelines, Recommendations, and Strength of the Evidence for Each Clinical Topic**

| Topic | Guidelines | Recommendations | Evidence Strength | | |
|---|---|---|---|---|---|
| | | | A | B | C |
| Clinical staging | 15 (29) | 74 (8) | 1 (1) | 14 (19) | 59 (80) |
| Diagnosis | 11 (22) | 40 (5) | 0 (0) | 8 (20) | 32 (80) |
| Follow-up/surveillance | 9 (18) | 29 (30) | 0 (0) | 2 (7) | 27 (93) |
| Initial evaluation/preparation | 7 (14) | 26 (3) | 0 (0) | 5 (19) | 21 (81) |
| Palliative care | 3 (6) | 8 (1) | 1 (12) | 2 (25) | 5 (63) |
| Palliative treatment | 5 (10) | 12 (1) | 2 (17) | 4 (33) | 6 (50) |
| Pathologic/surgical staging | 15 (29) | 61 (7) | 5 (8) | 10 (16) | 46 (75) |
| Practice organization | 6 (12) | 73 (8) | 3 (4) | 7 (10) | 63 (86) |
| Prevention | 7 (14) | 70 (8) | 25 (36) | 20 (29) | 25 (36) |
| Screening and early detection | 7 (14) | 14 (2) | 4 (29) | 1 (7) | 9 (64) |
| Treatment | | | | | |
| Small cell lung cancer | 14 (27) | 118 (13) | 18 (15) | 12 (10) | 88 (75) |
| Solitary pulmonary nodule | 4 (8) | 13 (1) | 0 (0) | 0 (0) | 13 (100) |
| Early stage | 2 (4) | 11 (1) | 4 (36) | 0 (0) | 7 (64) |
| Pancoast tumor, T4, special | 8 (16) | 25 (3) | 0 (0) | 4 (16) | 21 (84) |
| Stage I | 13 (26) | 42 (5) | 9 (21) | 9 (21) | 24 (57) |
| Stage II | 14 (27) | 56 (6) | 9 (16) | 15 (27) | 32 (57) |
| Stage IIIA/potentially resectable | 15 (29) | 61 (7) | 13 (21) | 9 (15) | 39 (64) |
| Stage IIIB/nonresectable | 16 (31) | 62 (7) | 12 (19) | 6 (10) | 44 (71) |
| Stage IV or IIIB with malignant pleural effusion | 21 (41) | 82 (9) | 16 (19) | 3 (4) | 63 (77) |
| Total | 51 | 880 | 122 (14) | 131 (15) | 627 (71) |

*Values given as No. (%). A = Strong evidence; B = weak evidence; C = consensus.

conflict of interest, specifically whether the guideline was editorially independent from the funding body and whether potential conflicts of interest were reported for the members of the guideline development group. The score in this domain was also poor, with a mean score of 24% (range, 0 to 83%). Four guidelines (8%) scored $\geq 50\%$. In 48 guidelines (94%), potential conflicts of interest on the part of guideline developers were not recorded.

*Overall Recommendations:* After reviewing all 51 guidelines and completing the AGREE instrument, the reviewers came to a consensus with respect to an overall recommendation for each guideline. As described in the "Materials and Methods" section, we recommended guidelines that we thought would be useful to health-care providers and that demonstrated good quality on the AGREE instrument. In total, we recommended 19 of 51 guidelines (37%). As noted in Table 3, for some guidelines (specifically, the British Thoracic Society recommendations to respiratory physicians for organizing the care of patients with lung cancer[34] and the Scottish Intercollegiate Guidelines Network guideline on the management of lung cancer[58]), we based our recommendation on the guidelines' superior performance on the AGREE instrument, while recognizing that many of the guideline statements specific to practice organization and review criteria would be directly relevant only within the system for which they were developed. Nonetheless, these documents serve as examples of well-constructed and well-communicated guidelines.

### *Agreement Among Reviewers*

Table 4 demonstrates both the degree of agreement beyond chance ($\kappa$ statistic) and the observed simple agreement among the reviewers for the 23 items of the AGREE instrument. The $\kappa$ values indicate that overall agreement was poor to fair for 65% of the items and was moderate to substantial for 35% of the items. Observed agreement among reviewers was high, with 74% of items having moderate-to-substantial agreement and 26% of items having excellent agreement. The degree of agreement appeared to be consistent across domains and did not appear to be correlated with domains that were quantitative vs qualitative in nature.

## Discussion

Over the past decade, a significant number of guidelines have been written and published on lung cancer diagnosis and treatment. In total, they cover a wide range of clinical topics with varying degrees of evidence to support their recommendations.

Although many of the guidelines are classified as

**Table 3—*AGREE Domain Scores for Clinical Practice Guidelines on Lung Cancer**

| Guideline | Scope and Purpose | Stakeholder Involvement | Rigor of Development | Clarity of Presentation | Applicability | Editorial Independence | Overall Recommendation |
|---|---|---|---|---|---|---|---|
| Practice guidelines in cardiothoracic surgery[12] | 31 | 17 | 11 | 48 | 4 | 13 | Would not recommend |
| ACS guidelines for the early detection of cancer; update of early detection guidelines for prostate, colorectal, and endometrial cancers; also update 2001—testing for early lung cancer detection[13] | 67 | 27 | 38 | 38 | 28 | 17 | Would not recommended |
| ACR Appropriateness Criteria: nonaggressive, nonsurgical treatment of inoperable non-small cell lung cancer[14] | 76 | 38 | 51 | 52 | 16 | 17 | Would not recommend |
| ACR Appropriateness Criteria: non-small cell lung cancer, nonsurgical, aggressive therapy[15] | 73 | 35 | 48 | 47 | 11 | 13 | Would not recommend |
| ACR Appropriateness Criteria: work-up of the solitary pulmonary nodule[16] | 76 | 35 | 49 | 48 | 13 | 13 | Would not recommend |
| ACR Appropriateness Criteria: follow-up and retreatment of brain metastases[17] | 69 | 31 | 42 | 48 | 6 | 8 | Would not recommend |
| ACR Appropriateness Criteria: follow-up of non-small cell lung cancer[18] | 73 | 38 | 49 | 52 | 16 | 17 | Would not recommend |
| ACR Appropriateness Criteria: multiple brain metastases[19] | 72 | 40 | 51 | 46 | 14 | 21 | Would not recommend |
| ACR Appropriateness Criteria: neoadjuvant therapy for marginally respectable (clinical N2) non-small cell lung cancer[20] | 75 | 38 | 51 | 50 | 14 | 21 | Would not recommend |
| ACR Appropriateness Criteria: postoperative radiotherapy in non-small cell lung canxcer[21] | 73 | 35 | 48 | 48 | 11 | 13 | Would not recommend |
| ACR Appropriateness Criteria: pre-irradiation evaluation and management of brain metastases[22] | 73 | 37 | 48 | 53 | 16 | 17 | Would not recommend |
| ACR Appropriateness Criteria: solitary brain metastasis[23] | 78 | 37 | 49 | 52 | 16 | 18 | Would not recommend |
| ACR Appropriateness Criteria: staging of bronchogenic carcinoma, non-small cell lung carcinoma[24] | 73 | 33 | 48 | 48 | 11 | 13 | Would not recommend |
| ACR Appropriateness Criteria: staging of non-small cell lung carcinoma[25] | 76 | 35 | 48 | 48 | 11 | 13 | Would not recommend |
| Consensus guidelines for high dose rate remote brachytherapy in cervical, endometrial, and endobronchial tumors[26] | 44 | 13 | 21 | 21 | 14 | 17 | Would not recommend |
| Clinical practice guidelines for the treatment of unresectable non-small cell lung cancer[27] | 96 | 70 | 95 | 85 | 49 | 63 | Recommend |
| Management of malignant pleural effusions[28] | 67 | 15 | 33 | 42 | 17 | 17 | Would not recommend |
| Guidelines for percutaneous transthoracic needle biopsy[29] | 64 | 23 | 8 | 48 | 6 | 17 | Would not recommend |
| Pretreatment evaluation of non-small-cell lung cancer[30] | 20 | 3 | 10 | 22 | 4 | 3 | Would not recommend |
| Oncology patient management guidelines: small cell lung cancer[31] | 62 | 17 | 17 | 62 | 13 | 13 | Would not recommend |
| Consensus statement on lung cancer[32] | 42 | 6 | 13 | 42 | 3 | 0 | Would not recommend |

**Table 3—*Continued**

| Guideline | Scope and Purpose | Stakeholder Involvement | Rigor of Development | Clarity of Presentation | Applicability | Editorial Independence | Overall Recommendation |
|---|---|---|---|---|---|---|---|
| BTS guidelines: guidelines on the selection of patients with lung cancer for surgery[33] | 94 | 54 | 89 | 79 | 33 | 83 | Recommend |
| BTS recommendations to respiratory physicians for organizing the care of patients with lung cancer[34] | 84 | 58 | 64 | 63 | 51 | 13 | Recommend† |
| The role of combination chemotherapy in the initial management of limited-stage small cell lung cancer[35] | 89 | 46 | 76 | 65 | 3 | 33 | Recommend |
| The role of single-agent docetaxel (Taxotere) as a second-line treatment for advanced non-small cell lung cancer[36] | 83 | 46 | 81 | 73 | 6 | 33 | Recommend |
| Altered fractionation of radical radiation therapy in the management of unresected non-small cell lung cancer | 94 | 48 | 94 | 67 | 42 | 42 | Recommend |
| Chemotherapy in stage IV (metastatic) non-small cell lung cancer[38] | 94 | 50 | 88 | 65 | 19 | 38 | Recommend |
| Postoperative adjuvant chemotherapy and/or radiation therapy in stage II or IIIA, completely resected non-small cell lung cancer[39] | 92 | 44 | 91 | 63 | 11 | 46 | Recommend |
| Prophylactic cranial irradiation in small cell lung cancer[40] | 92 | 54 | 87 | 71 | 8 | 33 | Recommend |
| The role of thoracic radiotherapy as an adjunct to standard chemotherapy in limited-stage small cell lung cancer[41] | 92 | 50 | 91 | 73 | 8 | 42 | Recommend |
| Unresected stage III non-small cell lung cancer[42] | 92 | 44 | 89 | 73 | 28 | 38 | Recommend |
| Use of gemcitabine in non-small cell lung cancer[43] | 78 | 42 | 81 | 56 | 25 | 38 | Recommend‡ |
| Use of preoperative chemotherapy with or without postoperative radiotherapy in technically resectable stage IIIA non-small cell lung cancer[44] | 92 | 40 | 91 | 65 | 8 | 46 | Recommend |
| Use of vinorelbine in non-small cell lung cancer[45] | 84 | 46 | 86 | 54 | 17 | 38 | Recommend‡ |
| Guidance on commissioning cancer services: improving outcomes in lung cancer; the manual[46] | 87 | 63 | 73 | 75 | 98 | 10 | Recommend |
| Clinical practice guidelines: smoking prevention and cessation[47] | 78 | 31 | 24 | 75 | 14 | 13 | Would not recommend |
| ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of non-small cell lung cancer[48] | 61 | 21 | 31 | 52 | 8 | 13 | Would not recommend |
| ESMO minimum clinical recommendations for diagnosis, treatment and follow-up of small cell lung cancer[49] | 53 | 21 | 30 | 58 | 22 | 21 | Would not recommend |
| Screening for lung cancer[50] | 72 | 19 | 26 | 65 | 39 | 17 | Would not recommend |
| Lung cancer (PDQ): prevention[51] | 58 | 21 | 44 | 46 | 17 | 17 | Would not recommend |
| Lung cancer (PDQ): screening[52] | 44 | 21 | 48 | 52 | 17 | 17 | Would not recommend |
| Non-small cell lung cancer (PDQ): treatment[53] | 44 | 13 | 13 | 45 | 2 | 10 | Would not recommend |

**Table 3—*Continued**

| Guideline | Scope and Purpose | Stakeholder Involvement | Rigor of Development | Clarity of Presentation | Applicability | Editorial Independence | Overall Recommendation |
|---|---|---|---|---|---|---|---|
| Small cell lung cancer (PDQ): treatment[54] | 53 | 21 | 49 | 56 | 14 | 17 | Would not recommend |
| NCCN practice guidelines for non-small cell lung cancer[55] | 53 | 22 | 21 | 72 | 4 | 7 | Would not recommend |
| NCCN practice guidelines for small cell lung cancer[56] | 56 | 15 | 21 | 65 | 2 | 7 | Would not recommend |
| Guidelines on the nonsurgical management of lung cancer[57] | 92 | 52 | 79 | 90 | 64 | 67 | Recommend |
| Management of lung cancer: a national clinical guideline recommended for use in Scotland[58] | 83 | 63 | 79 | 77 | 67 | 25 | Recommend |
| Lung cancer surgical practice guidelines[59] | 64 | 21 | 2 | 29 | 0 | 17 | Would not recommend |
| Workshop on consensus guidelines for management of lung cancer[60] | 61 | 31 | 14 | 15 | 14 | 0 | Would not recommend |
| Treating tobacco use and dependence[61] | 97 | 63 | 94 | 88 | 61 | 79 | Recommend |
| Screening for lung cancer[62] | 78 | 27 | 70 | 69 | 19 | 25 | Recommend |
| Means | 72 | 35 | 52 | 57 | 20 | 24 | |

*Values given as percentage. See Table 1 for abbreviations not used in text.
†Recommended based upon AGREE. Recommendations may not be relevant outside of the United Kingdom.
‡Recommended based upon AGREE. Utility of guidelines for single agent questionable.

evidence-based, a thorough review of their quality utilizing the AGREE instrument led the authors to recommend fewer than half of the guidelines. The reasons for this are multifactorial. Overall, almost all the guidelines performed poorly with respect to applicability and editorial independence. Even those guidelines that explicitly based their recommendations on evidence, such as those developed by the Cancer Care Ontario Practice Guidelines Initiative,[35–45] failed to address issues of barriers to implementation, monitoring criteria, and evidence of pilot testing. Addressing such issues is necessary if the guideline movement is to continue successfully. Although few studies have assessed the impact of guideline development on patient outcomes,[63] it has been demonstrated that explicit guidelines can improve clinical practice; however, improvement requires rigorous evaluation. Well-developed guidelines should include the consideration of potential barriers to guideline implementation, should supply monitoring criteria to assess the guideline's impact, and should provide evidence of pilot testing to ensure that the guideline can be practically put to clinical use.

**Table 4—*Agreement Among Reviewers for AGREE Instrument Items***

| Strength of Agreement | Agreement | Items, No. κ Statistic | Items, No. Simple Agreement |
|---|---|---|---|
| Poor | <0.00 | 1 | 0 |
| Slight | 0.00–0.20 | 7 | 0 |
| Fair | 0.21–0.40 | 7 | 0 |
| Moderate | 0.41–0.60 | 7 | 3 |
| Substantial | 0.61–0.80 | 1 | 14 |
| Excellent | >0.80 | 0 | 6 |

Another area where the lung cancer guidelines consistently failed to perform was in the domain of editorial independence. Poor performance in this domain could represent true conflicts of interest between funding sources and guideline development panels; alternatively, it may simply reflect poor reporting on these topics. The developers of the AGREE instrument contacted the authors of each guideline they reviewed to obtain background material that could inform the reviewers' ratings. For some items, this additional communication may have provided more information than we were able to obtain from reviewing the guidelines and any accompanying material we could obtain from additional references or the World Wide Web. For the lung cancer guidelines, documentation regarding the issue of an individual's conflict of interest was rarely stated. Explicit statements about whether or not the funding body was independent editorially from the guideline committee were also infrequent. Therefore, poor performance in this domain could have been due to our failure to obtain further information from each guideline author. However, future guideline efforts would benefit from clear documentation on this matter within the text of the guideline document so that readers will be able to determine for themselves whether or not a conflict of interest potentially exists.

One of the key factors regarding the adequacy of the guidelines pertains to the rigor of development. Despite the fact that most of the guidelines included references to published literature, many did not clearly delineate the literature review methodology used or the mechanism by which recommendations were formulated. This step is crucial in determining whether the recommendations are truly based on the evidence and in understanding how the evidence is synthesized.

Patient preferences and experiences should be factored into decisions regarding clinical care, especially in diseases such as lung cancer in which treatments can have significant morbidity and can impact on quality of life. Almost all of the guidelines we reviewed would have benefited from more attention to this issue. This could be accomplished by ensuring that all guideline committees have patient representatives and that literature reviews specifically address quality of life when available. It would also be helpful if greater efforts were made in the research community to ensure that quality of life and patient preferences are incorporated into research protocols.

Implementation of practice guidelines also requires attention to local practice patterns. For example, the Cancer Guidance Group[46] guideline provides specific implementation strategies and review criteria for their recommendations. Many of these strategies and some of the corresponding monitoring criteria are specific to the United Kingdom. Nonetheless, this guideline provides an example of items that should be incorporated by those undertaking a guideline effort. Furthermore, those looking to apply currently available guidelines can learn from their detailed efforts to address implementation issues and adapt what is relevant locally.

The recommendations that result from interpretation of the evidence also can vary among guidelines. This variation could be a function of local bias, difference in data interpretation, or a manifestation of available resources. Nonetheless, one needs to be careful when considering other's guidelines for local use and needs to ensure that the clinical data are concordant with the evidence and clinical judgment. Because of the variability noted in guidelines that referenced the same studies, it is crucial that a guideline effort have a clear methodology for going from the evidence to the recommendations so that the possibility of bias is minimized.

In this study, many of the conclusions are based on a review utilizing the AGREE instrument. Although this instrument is fairly new, it is one of the few guideline assessment tools to demonstrate validity and reliability. Furthermore, the areas covered by the instrument are logical for anyone to consider when conducting guideline development or evaluation. A guideline that addresses the issues raised by the AGREE instrument is more likely to be a rigorously developed guideline. Nevertheless, the AGREE instrument has some limitations. For one, the interrater reliability was primarily slight to moderate. Some of the variability may be due to differences in interpretation of several items where the instructions were broad. For example, for item 22, which is contained within the domain of editorial independence, the $\kappa$ statistic was only 0.14. This slight agreement probably arises from the fact that this question, which asks whether or not the guideline is editorially independent from the funding body, is open to interpretation, with some reviewers stating that the criterion was not met unless the statement was explicitly made in the guideline, while others interpreted the criterion to be met if the funding agency was the government, as in several of the UK and Canadian guidelines.[34–45,58] However, in this case, the simple agreement was still 58%. In contrast, for item 12, which addresses whether or not there is an explicit link between the recommendations and the supporting evidence, the $\kappa$ statistic was $> 0.6$. This is not unexpected, given that this item is relatively straightforward. The issue of low interrater reliability was observed in the previous version of this instrument[64] and was accommodated by the use of multiple reviewers, as well as through the refinement of the instrument's questions and instructions. Moreover, the degree of agreement among raters was good, with all items having moderate or better agreement.

Another potential limitation of the AGREE instrument concerns the validity of the responses to the question on the overall assessment of the guideline. Although the reviewers were instructed to consider the domain scores when making a decision about whether or not to recommend the guideline, no clear rules were established as to how to weight the differing domains. However, when reviewing the assessments compared with the domain scores, the responses appear to have validity. For each guideline that was recommended, the overall domain scores were $> 50\%$ for at least three domains, with an average of four domains with a score of $> 50\%$. For guidelines that were not recommended, on average only 1.3 domains had a score of $> 50\%$. Furthermore, the score on the domain "rigor of development" for recommended guidelines was high. All scores were $> 50\%$, with an average score of 84%. Conversely, for guidelines we did not recommend, the average score for this domain was only 33%.

In conclusion, a review of current lung cancer guidelines demonstrates that many of the clinical

topics of interest have been considered by at least one guideline. None covers all the necessary elements. Furthermore, although prior guidelines may accurately reflect clinical practice, few adhere to the standards set forth by the AGREE instrument. A guideline effort for lung cancer, which adheres to all the criteria explicit in the AGREE instrument and clearly addresses each item in the guideline text, would add substantially to the literature.

## Appendix: AGREE Instrument*

Response categories for each question are as follows:

1. Strongly disagree
2. Disagree
3. Agree
4. Strongly agree

*Scope and Purpose*

1. The overall objectives of the guideline are specifically described.
2. The clinical questions covered by the guideline are specifically described.
3. The patients to whom the guideline is meant to apply are specifically described.

*Stakeholder Involvement*

4. The guideline development group includes individuals from all the relevant professional groups.
5. The patients' views and preferences have been sought.
6. The target users of the guideline are clearly defined.
7. The guideline has been piloted among end-users.

*Rigor of Development*

8. Systematic methods were used to search for evidence.
9. The criteria for selecting the evidence are clearly described.
10. The methods used for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline was externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.

*Clarity and Presentation*

15. The recommendations are specific and unambiguous.
16. The different options for management of the condition are clearly presented.
17. Key recommendations are easily identifiable.
18. The guideline is supported with tools for application.

*Applicability*

19. The potential organizational barriers in applying the recommendations have been discussed.
20. The potential cost implications of applying the recommendations have been considered.
21. The guideline presents key review criteria for monitoring and/or audit purposes.

*Editorial Independence*

22. The guideline is editorially independent from the funding body.
23. Conflicts of interest of the guideline development members have been recorded.

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ACKNOWLEDGMENT: The authors would like to acknowledge Gregory P. Samsa, PhD, for help with statistical analysis.

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