Complete Summary

GUIDELINE TITLE

The diagnosis and treatment of lung cancer.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Acute Care. The diagnosis and treatment of lung cancer. London (UK): National Institute for Clinical Excellence (NICE); 2005 Feb. 350 p.

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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

SCOPE

DISEASE/CONDITION(S)

Lung cancer (including small cell lung cancer and non small cell lung cancer)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Geriatrics
Internal Medicine
Nuclear Medicine
Nursing
Oncology
Pathology
Psychology
Pulmonary Medicine
Radiation Oncology
Radiology
Thoracic Surgery

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Dietitians
Health Care Providers
Hospitals
Nurses
Occupational Therapists
Patients
Pharmacists
Physical Therapists
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Public Health Departments
Respiratory Care Practitioners
Social Workers

GUIDELINE OBJECTIVE(S)

To offer the best practice advice on the care of adults who are suspected of having, or are diagnosed with, lung cancer

TARGET POPULATION

Adults over the age of 18 years who are suspected as having, or are diagnosed with lung cancer (including small cell lung cancer and non small cell lung cancer)

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis and Staging

1. General
    - Providing information to patients on all aspects of their diagnosis, treatment and care
    - Discussing treatment options and plans with patients, with joint decision making

- Medical history and physical examination
- Assessment of comorbid conditions
- Assessment of major prognostic factors (performance status, serum lactate dehydrogenase, liver function tests, serum sodium, and stage [for small cell lung cancer])

2. Imaging
    - Chest x-ray
    - Computed tomography (CT)
    - ^{18}F-deoxyglucose positron emission tomography (FDG-PET)
    - NeoSPECT (Technetium-99m depreotide) scanning
    - Ultrasound (US)
    - Magnetic resonance imaging (MRI)
    - Imaging of specific sites of metastasis (brain, liver, adrenals, bone)
3. Invasive and tissue confirmation
    - Percutaneous transthoracic needle aspiration/biopsy
    - Biopsy of site other than the lung
    - Surgical biopsy
    - Sputum cytology
    - Bronchoscopy (with biopsy and cytology sampling)
    - Thoracoscopy
    - Pleural tap and pleural fluid cytology
    - Mediastinoscopy/mediastinotomy
    - Endoscopic ultrasound guided fine needle aspiration (EUS-FNA)
    - Transbronchial needle aspiration (TBNA)

Treatment

1. Surgery
    - Criteria for patient selection (including comorbidities, pulmonary function, and disease stage)
    - Pneumonectomy
    - Standard and extended lobectomy
    - Sub lobar resection (e.g., wedge resection)
    - Video-assisted thoracoscopic surgery
    - Lymph node sampling
2. Radiotherapy
    - Radical (continuous, hyperfractioned, accelerated radiotherapy (CHART), conventional)
    - Palliative radiotherapy
    - Prophylactic cranial irradiation (for SCLC)
3. Chemotherapy
    - Docetaxel
    - Paclitaxel
    - Gemcitabine
    - Vinorelbine
    - Ifosfamide
    - Vinblastine
    - Vindesine
    - Mitomycin C
    - Carboplatin
    - Cisplatin
4. Combination treatments

    - Pre-operative chemotherapy
    - Post-operative chemotherapy
    - Pre-operative radiotherapy
    - Post-operative radiotherapy
    - Post-operative chemoradiotherapy
    - Sequential radiotherapy
    - Concurrent radiotherapy
5. Endobronchial treatment as a radical treatment
    - Photodynamic therapy
    - Brachytherapy
    - Electrocautery
    - Cryotherapy
    - Laser ablation

Palliative Care

1. External beam radiotherapy
2. Opioids (codeine or morphine)
3. Debulking bronchoscopic procedures
4. Corticosteroids (for cerebral metastases)
5. Non-drug interventions (psychosocial support, breathing control and coping strategies for patients with breathlessness)
6. Referral to appropriate specialist
7. Pleural aspiration/drainage
8. Talc pleurodesis
9. Endobronchial therapy
    - Photodynamic therapy
    - Brachytherapy
    - Stenting (including superior vena cava (SVC) stenting)
    - Laser therapy
    - Cryotherapy
    - Diathermy
10. Physical and Psychological Support
    - Physiotherapy
    - Occupational therapy
    - Psychological and spiritual support
    - End of life/bereavement care

Service Organisation

1. Multi-disciplinary teams
2. Early diagnosis clinics
3. Specialist nurse support
4. Timing of treatment
5. Patient follow-up

MAJOR OUTCOMES CONSIDERED

- Morbidity and mortality
- Side effects of medications and interventions
- Sensitivity and specificity of diagnostic tests
- Quality of life

- Cost measures, including cost effectiveness
- Quality adjusted life years

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

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

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Searches were performed using generic and specific filters, relevant medical subject heading terms and free text terms. Only studies on patients with lung cancer (or where the majority of patients recruited were those with lung cancer) were included, with one exception. When the treatment of pleural effusion was considered, studies on patients with mixed primary sites were included as specific data was not available and the Guideline Development Group (GDG) agreed that the site of the primary tumour would not determine treatment in this case. Details of all literature searches are available in appendix six of the full version of the original guideline document. The scope and the clinical questions can be found in appendix seven and eight of the original guideline document (full version) respectively.

Search filters to identify systematic reviews, randomised controlled trials and observational studies were adapted from the Scottish Intercollegiate Guideline Network (SIGN) methodological search filters (http://www.sign.ac.uk/methodology/filters.html). The lung cancer search strategy stem was devised in collaboration with SIGN. It was then combined with independently devised search strategies for each section of the guideline. The following databases were searched for all section:

- The Cochrane Library (up to Issue 4, 2003)
- Medline (OVID) 1966-2003 (week 52)
- Embase (OVID) 1980-2003 (week 52)

The Cumulative Index to Nursing and Allied Health Literature (CINAHL) and PsychInfo were also searched for relevant clinical questions. Identification of high quality systematic reviews determined the date ranges searched for each clinical question. No language restrictions were applied to the search but identified foreign papers were not requested or reviewed. The cut off date for the National Collaborating Centre for Acute Care (NCC-AC) literature search was 31st December 2003. In order to be consistent and systematic the guideline developers did not consider papers after this date. This decision was made for pragmatic reasons of workload and meant that very current data was missed.

There was no systematic attempt to search for all the 'grey literature' (conferences, abstracts, theses and unpublished literature). However, the American Society of Clinical Oncology (ASCO) (http://www.asco.org) was searched for interventional abstracts to identify and verify published papers. Guidelines and reports from relevant websites, (including the following listed

below) were searched for. Bibliographies of identified reports and guidelines were also checked to identify relevant literature.

- National Institute for Health and Clinical Excellence (NICE) (www.nice.org.uk)
- National electronic Library for Health (NeLH) (http://www.nelh.nhs.uk/)
- National Institutes of Health Consensus Development Program (consensus.nih.gov)
- New Zealand Guidelines Development Group (NZGG) (http://www.nzgg.org.nz/)
- Scottish Intercollegiate Guideline Network (SIGN) (www.sign.ac.uk)
- US National Guideline Clearinghouse (www.guideline.gov)
- Google (www.google.com)

All retrieved articles were methodologically appraised using checklists developed by SIGN.

All relevant guidelines issued by the American College of Chest Physicians (ACCP), the British Thoracic Society a Health Technology Board for Scotland (HTBS) report (on the staging of lung cancer) were included in the evaluation.

Literature Review for Health Economics

Published economic evidence was obtained from a systematic search of the following databases:

- Medline (Ovid) (1966-2003)
- Embase (1980-2003)
- Health Economic Evaluations Database (HEED)
- NHS Economic Evaluations Database (NHS EED)

For those clinical areas that were reviewed, the information scientists used the same search strategy as for the clinical questions, substituting an economics filter for a study type filter. For those clinical areas SIGN reviewed, the information scientists had to design a filter specifically for the health economists.

Each search strategy was designed to find any applied study estimating the cost or cost-effectiveness of some aspect of lung cancer. A health economist reviewed abstracts and database reviews of papers. Relevant references in the bibliographies of reviewed papers were also identified and reviewed.

Given the diversity of economic studies, it was not possible to determine a general exclusion criterion based on study quality. Hence all studies were included in the evidence tables (including abstracts) and study quality and applicability are discussed in the review. Papers were only excluded from the evidence tables and review if:

- Results were not reported specifically for lung cancer patients (Although occasionally studies were found and included, where most but not all patients had lung cancer, e.g. in comparisons of different types of thoracic surgery).
- The study did not contain any original data on cost or cost-effectiveness (i.e. it was a review or a clinical paper).

- The analysis was not incremental and was not described adequately to allow incremental analysis (so studies reporting only average cost-effectiveness ratios were excluded unless they provided data to allow the calculation of incremental cost-effectiveness ratios).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence for Intervention Studies

1++: High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1 -: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++: High quality systematic reviews of case-control or cohort studies

High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal

2+: Well-conducted case-control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal

2-: Case control or cohort studies with a high risk of confounding, bias and a significant risk that the relationship is not causal

3: Non-analytic studies (for example, case reports, case series)

4: Expert opinion

Levels of Evidence for Studies of Diagnostic Tests

Ia: Systematic review (with homogeneity)* of level-1 studies**

Ib: Level-1 studies**

II: Level-2 studies*** Systematic reviews of level-2 studies

III: Level-3 studies**** Systematic reviews of level-3 studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience without explicit critical experience, based on physiology, bench research, or first principles.

*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

**Level-1 studies are studies:

- That use a blind comparison of the test with a validated reference standard (gold standard)
- In a sample of patients that reflects the population to whom the test would apply.

***Level-2 studies are studies that have **only one** of the following:

- Narrow population (the sample does not reflect the population to whom the test would apply)
- Use a poor reference standard (defined as that where the "test" is included in the "reference", or where the "testing" affects the "reference")
- The comparison between the test and reference is not blind
- Case-control studies

****Level-3 studies are studies that have **at least two or three** of the features listed above.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The aim of the literature review was to identify and synthesise relevant evidence within the published literature, in order to answer specific clinical questions.

For each clinical question the highest level of evidence was sought. Studies that were assessed to be of adequate quality were summarised in evidence tables. All the evidence tables can be found in appendix one of the original guideline document.

For studies of diagnostic accuracy the sensitivity, specificity, positive predictive value (PPV) and the negative predictive value (NPV) were reported.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The Guideline Development Group was presented with summaries (text and evidence tables) of the best available research evidence to answer the clinical questions. Recommendations were based on, and explicitly linked to, the evidence that supported them. The evidence tables can be found in appendix one of the original guideline document.

The Group worked on an informal consensus basis. The recommendations were then graded according to the level of evidence upon which they were based.

Recommendations based on studies assessing the diagnostic accuracy of tests are also classified according to the strength of the supporting evidence. The classification system used for diagnostic tests is currently being piloted and has not yet been systematically tested by the National Institute for Health and Clinical Excellence (NICE). Some recommendations in this guideline have two grades because they are based on both diagnostic and effectiveness evidence.

The usefulness of a classification system based solely on the level of evidence has been questioned because it does not take into consideration the importance of the recommendation in changing practice and improving patient care. It is worth noting that NICE is currently assessing the best way of presenting recommendations for future guidelines.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grading of Recommendations on Interventions

Grade A:

- At least one meta-analysis, systematic review, or randomized control trial (RCT) rated as 1++, and directly applicable to the target population, or
- A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
- Evidence drawn from a National Institute for Health and Clinical Excellence (NICE) technology appraisal

Grade B:

- A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 1++ or 1+

Grade C:

- A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 2++

Grade D:

- Evidence level 3 or 4, or
- Extrapolated evidence from studies rated as 2+, or
- Formal consensus

D (GPP):

A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Grading of Recommendations on Diagnostic Tests

Grade A (DS): Studies with level of evidence Ia or Ib

Grade B (DS): Studies with level of evidence II

Grade C (DS): Studies with level of evidence III

Grade D (DS): Studies with level of evidence IV

(DS = diagnostic studies)

COST ANALYSIS

Cost-Effectiveness Modelling

Specific topics were selected for original economic analysis if there was a likelihood that the recommendation made would substantially change clinical practice in the National Health Service (NHS) and have important consequences for resource use.

In three cases there was not a relevant economic evaluation in the published literature: continuous, hyperfractioned, accelerated radiotherapy (CHART), versus conventional radical radiotherapy for non-small cell lung cancer (NSCLC); ^{18}F-deoxyglucose positron emission tomography (FDG-PET) in the work-up to radical radiotherapy for NSCLC; and platinum versus non-platinum drug regimens in the treatment of small cell lung cancer (SCLC).

In a fourth case, economic evaluations had been previously published but had substantial limitations - FDG-PET in the work-up to curative surgery for NSCLC.

Methods used depended on the question being analysed, however, the following principles were followed:

- The guideline development group (GDG) was consulted during the construction and interpretation of each model.
- Each model was based on the best evidence from the systematic review.
- Model assumptions were reported fully and transparently.

- The results were subject to thorough sensitivity analysis and limitations discussed.
- Costs were calculated from a health services perspective.

A full description of the results from the cost analysis is presented in a report that is available from the National Institute for Health and Clinical Excellence (NICE) Web site.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The first draft of the guideline (The full guideline, National Institute for Health and Clinical Excellence (NICE) guideline and Quick Reference Guide) were consulted with Stakeholders and comments were considered by the Guideline Development Group (GDG).

The final consultation draft of the Full guideline, the NICE guideline and the Information for the Public were submitted to stakeholders for final comments.

The final draft was submitted to the Guideline Review Panel for review prior to publication.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The strength of recommendation grading (A-D (GPP)) and level of evidence (1++-4) for interventional studies and strength of recommendation grading A (DS) - D (DS) and level of evidence (Ia - IV) for diagnostic studies are defined at the end of the "Major Recommendations" field.

Access to Services

D (GPP) - All patients diagnosed with lung cancer should be offered information, both verbal and written, on all aspects of their diagnosis, treatment and care. This information should be tailored to the individual requirements of the patient, and audio and videotaped formats should also be considered.

D (GPP) - Treatment options and plans should be discussed with the patient and decisions on treatment and care should be made jointly with the patient. Treatment plans must be tailored around the patient's needs and wishes to be involved, and his or her capacity to make decisions.

D (GPP) - The public needs to be better informed of the symptoms and signs that are characteristic of lung cancer, through co-ordinated campaigning to raise awareness.

D - Urgent referral for a chest X-ray should be offered when a patient presents with:

- haemoptysis, or
- any of the following unexplained or persistent (that is, lasting more than 3 weeks) symptoms or signs:
    - cough
    - chest/shoulder pain
    - dyspnoea
    - weight loss
    - chest signs
    - hoarseness
    - finger clubbing
    - features suggestive of metastasis from a lung cancer (for example in brain, bone, liver or skin)
    - cervical/supraclavicular lymphadenopathy

D - If a chest X-ray or chest computerised tomography (CT) scan suggests lung cancer (including pleural effusion and slowly resolving consolidation), patients should be offered an urgent referral to a member of the lung cancer multidisciplinary team (MDT), usually a chest physician.

D - If the chest X-ray is normal but there is a high suspicion of lung cancer, patients should be offered urgent referral to a member of the lung cancer MDT, usually the chest physician.

D - Patients should be offered an urgent referral to a member of the lung cancer MDT, usually the chest physician, while awaiting the result of a chest X-ray, if any of the following are present:

- persistent haemoptysis in smokers/ex-smokers over 40 years of age
- signs of superior vena caval obstruction (swelling of the face/neck with fixed elevation of jugular venous pressure)
- stridor

Emergency referral should be considered for patients with superior vena cava obstruction or stridor.

Diagnosis

D (GPP) - Where a chest X-ray has been requested in primary or secondary care and is incidentally suggestive of lung cancer, a second copy of the radiologist's report should be sent to a designated member of the lung cancer MDT, usually the chest physician. The MDT should have a mechanism in place to follow up these reports to enable the patient's General Practitioner (GP) to have a management plan in place.

D (GPP) - Patients with known or suspected lung cancer should be offered a contrast-enhanced chest CT scan to further the diagnosis and stage the disease. The scan should also include the liver and adrenals.

Chest CT should be performed before:

- **A; C(DS)** - an intended fibreoptic bronchoscopy
- **D (GPP)** - any other biopsy procedure

B (DS) - Bronchoscopy should be performed on patients with central lesions who are able and willing to undergo the procedure.

B (DS) - Sputum cytology is rarely indicated and should be reserved for the investigation of patients who have centrally placed nodules or masses and are unable to tolerate, or unwilling to undergo, bronchoscopy or other invasive tests.

B (DS) - Percutaneous transthoracic needle biopsy is recommended for diagnosis of lung cancer in patients with peripheral lesions.

B (DS) - Surgical biopsy should be performed for diagnosis where other less invasive methods of biopsy have not been successful or are not possible.

D (GPP) - Where there is evidence of distant metastases, biopsies should be taken from the metastatic site if this can be achieved more easily than from the primary site.

C; B (DS) - An ^{18}F-deoxyglucose positron emission tomography (FDG-PET) scan should be performed to investigate solitary pulmonary nodules in cases where a biopsy is not possible or has failed, depending on nodule size, position and CT characterisation.

Staging

Non-Small Cell Lung Cancer (NSCLC)

In the assessment of mediastinal and chest wall invasion:

- **B (DS)** - CT alone may not be reliable
- **D (GPP)** - other techniques such as ultrasound should be considered where there is doubt
- **D (GPP)** - surgical assessment may be necessary if there are no contraindications to resection.

C (DS) - Magnetic resonance imaging (MRI) should not routinely be performed to assess the stage of the primary tumour (T-stage) in NSCLC.

B (DS) - MRI should be performed, where necessary to assess the extent of disease, for patients with superior sulcus tumours.

D (GPP) - Every cancer network should have a system of rapid access to FDG-PET scanning for eligible patients.

A (DS) - Patients who are staged as candidates for surgery on CT should have an FDG-PET scan to look for involved intrathoracic lymph nodes and distant metastases.

D (GPP)- Patients who are otherwise surgical candidates and have, on CT, limited (1-2 stations) N2/3 disease of uncertain pathological significance should have an FDG-PET scan.

B (DS) - Patients who are candidates for radical radiotherapy on CT should have an FDG-PET scan.

A - Patients who are staged as N0 or N1 and M0 (stages I and II) by CT and FDG-PET and are suitable for surgery should not have cytological/histological confirmation of lymph nodes before surgical resection.

B (DS) - Histological/cytological investigation should be performed to confirm N2/3 disease where FDG-PET is positive. This should be achieved by the most appropriate method. Histological/cytological confirmation is not required:

- where there is definite distant metastatic disease
- where there is a high probability that the N2/N3 disease is metastatic (for example, if there is a chain of high FDG uptake in lymph nodes).

B (DS) - When an FDG-PET scan for N2/N3 disease is negative, biopsy is not required even if the patient's nodes are enlarged on CT.

D (GPP) - If FDG-PET is not available, suspected N2/3 disease, as shown by CT scan (nodes with a short axis > 1cm), should be histologically sampled in patients being considered for surgery or radical radiotherapy.

D (GPP) - An MRI or CT scan should be performed for patients with clinical signs or symptoms of brain metastasis.

D (GPP) - An X-ray should be performed in the first instance for patients with localised signs or symptoms of bone metastasis. If the results are negative or inconclusive, either a bone scan or an MRI scan should be considered.

Small Cell Lung Cancer

D (GPP) - SCLC should be staged by a contrast-enhanced CT scan of the patient's chest, liver and adrenals and by selected imaging of any symptomatic area.

Surgery with Curative Intent for Patients with NSCLC

D - Surgical resection is recommended for patients with stage I or II NSCLC who have no medical contraindications and adequate lung function.

C - For patients with stage I or II NSCLC who can tolerate lobar resection, lobectomy is the procedure of choice.

D - Pending further research, patients with stage I or II NSCLC who would not tolerate lobectomy because of comorbid disease or pulmonary compromise should be considered for limited resection or radical radiotherapy.

D (GPP) - For all patients with stage I or II NSCLC undergoing surgical resection -- usually a lobectomy or a pneumonectomy -- clear surgical margins should be the aim.

C - Sleeve lobectomy offers an acceptable alternative to pneumonectomy for patients with stage I or II NSCLC who have an anatomically appropriate (central) tumour. This has the advantage of conserving functioning lung.

C - For patients with T3 NSCLC with chest wall involvement who are undergoing surgery, complete resection of the tumour should be the aim by either extrapleural or en bloc chest wall resection.

D (GPP) - All patients undergoing surgical resection for lung cancer should have systematic lymph node sampling to provide accurate pathological staging.

D (GPP) - In patients with stage IIIA (N2) NSCLC detected through preoperative staging, surgery alone is associated with a relatively poor prognosis. Therefore, these patients should be evaluated by the lung cancer MDT.

Radical Radiotherapy Alone for Treatment of NSCLC

D (GPP) - Radical radiotherapy is indicated for patients with stage I, II or III NSCLC who have good performance status (WHO 0, 1) and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage.

D (GPP) - All patients should undergo pulmonary function tests (including lung volumes and transfer factor) before having radical radiotherapy for NSCLC.

D (GPP) - Patients who have poor lung function but are otherwise suitable for radical radiotherapy should still be offered radiotherapy, provided the volume of irradiated lung is small.

A - Patients with stage I or II NSCLC who are medically inoperable but suitable for radical radiotherapy should be offered the CHART regimen.

A - Patients with stages IIIA or IIIB NSCLC who are eligible for radical radiotherapy and who cannot tolerate or do not wish to have chemoradiotherapy should be offered the CHART regimen.

D (GPP) - If CHART is not available, conventionally fractionated radiotherapy to a dose of 64 to 66 Gy in 32 to 33 fractions over 6 1/2 weeks or 55 Gy in 20 fractions over 4 weeks should be offered.

Chemotherapy for NSCLC

A - Chemotherapy should be offered to patients with stage III or IV NSCLC and good performance status (WHO 0, 1 or a Karnofsky score of 80-100), to improve survival, disease control and quality of life.

D (GPP) - Chemotherapy for advanced NSCLC should be a combination of a single third-generation drug (docetaxel, gemcitabine, paclitaxel or vinorelbine) plus a platinum drug. Either carboplatin or cisplatin may be administered, taking account of their toxicities, efficacy and convenience.

A - Patients who are unable to tolerate a platinum combination may be offered single-agent chemotherapy with a third-generation drug.

A - Docetaxel monotherapy should be considered if second-line treatment is appropriate for patients with locally advanced or metastatic NSCLC in whom relapse has occurred after previous chemotherapy.

The development of this section included a review of the following technology appraisal. "Docetaxel, paclitaxel, gemcitabine and vinorelbine for non-small cell lung cancer. NICE Technology Appraisal No. 26 (2001)". The appraisal is therefore now obsolete and has been replaced by the guideline.

Combination Treatment for NSCLC

B - Patients with stage I, II or IIIA NSCLC who are suitable for resection should not be offered preoperative chemotherapy unless it is part of a clinical trial.

A - Preoperative radiotherapy is not recommended for patients with NSCLC who are able to have surgery.

A - Postoperative radiotherapy is not recommended for patients with NSCLC after complete resection.

D - Postoperative radiotherapy should be considered after incomplete resection of the primary tumour for patients with NSCLC, with the aim of improving local control.

A - Adjuvant chemotherapy should be offered to NSCLC patients who have had a complete resection, with discussion of the risks and benefits.

B - Patients who are pathologically staged as II and III NSCLC following resection should not receive postoperative chemoradiotherapy unless it is within a clinical trial.

A - Patients with stage III NSCLC who are not suitable for surgery but are eligible for radical radiotherapy should be offered sequential chemoradiotherapy.

Treatment of Small Cell Lung Cancer (SCLC)

D - Patients with SCLC should be offered an assessment that includes evaluation of the major prognostic factors: performance status, serum lactate dehydrogenase, liver function tests, serum sodium, and stage.

All patients with SCLC should be offered:

- **A** - platinum-based chemotherapy

- **A** - multidrug regimens, because they are more effective and have a lower toxicity than single-agent regimens.

A - Four to six cycles of chemotherapy should be offered to patients whose disease responds. Maintenance treatment is not recommended.

A - Patients with limited-stage SCLC should be offered thoracic irradiation concurrently with the first or second cycle of chemotherapy or following completion of chemotherapy if there has been at least a good partial response within the thorax. For patients with extensive disease, thoracic irradiation should be considered following chemotherapy if there has been a complete response at distant sites and at least a good partial response within the thorax.

D (GPP) - Patients undergoing consolidation thoracic irradiation should receive a dose in the range of 40 Gy in 15 fractions over 3 weeks to 50 Gy in 25 fractions over 5 weeks.

A - Patients with limited disease and complete or good partial response after primary treatment should be offered prophylactic cranial irradiation.

D (GPP) - Second-line chemotherapy should be offered to patients at relapse only if their disease responded to first-line chemotherapy. The benefits are less than those of first-line chemotherapy.

Palliative Interventions and Supportive and Palliative Care

This section focuses on palliative interventions and supportive and palliative care for patients with lung cancer and therefore only evidence specific to lung cancer was reviewed. An absence of evidence does not imply that nothing can be done to help, and supportive and palliative care multidisciplinary teams - in particular specialist palliative care teams - have an important role in symptom control.

D (GPP) - Supportive and palliative care of the patient should be provided by general and specialist palliative care providers in accordance with the NICE guidance "Improving supportive and palliative care for adults with cancer."

D (GPP) - Patients who may benefit from specialist palliative care services should be identified and referred without delay.

A - External beam radiotherapy should be considered for the relief of breathlessness, cough, haemoptysis or chest pain.

A - Opioids, such as codeine or morphine, should be considered to reduce cough.

D - Debulking bronchoscopic procedures should be considered for the relief of distressing large-airway obstruction or bleeding due to an endobronchial tumour within a large airway.

D - Patients with endobronchial symptoms that are not palliated by other means may be considered for endobronchial therapy.

D - Patients with extrinsic compression may be considered for treatment with stents.

A - Non-drug interventions based on psychosocial support, breathing control and coping strategies should be considered for patients with breathlessness.

D (GPP) - Non-drug interventions for breathlessness should be delivered by a multidisciplinary group, co-ordinated by a professional with an interest in breathlessness and expertise in the techniques (for example, a nurse, physiotherapist or occupational therapist). Although this support may be provided in a breathlessness clinic, patients should have access to it in all care settings.

D (GPP) - Patients with troublesome hoarseness due to recurrent laryngeal nerve palsy should be referred to an ear, nose and throat specialist for advice.

A - Patients who present with superior vena cava obstruction should be offered chemotherapy and radiotherapy according to the stage of disease and performance status.

B - Stent insertion should be considered for the immediate relief of severe symptoms of superior vena caval obstruction or following failure of earlier treatment.

D - Corticosteroids and radiotherapy should be considered for symptomatic treatment of cerebral metastases in lung cancer.

D (GPP) - Other symptoms, including weight loss, loss of appetite, depression and difficulty swallowing, should be managed by multidisciplinary groups that include supportive and palliative care professionals.

B - Pleural aspiration or drainage should be performed in an attempt to relieve the symptoms of a pleural effusion.

B - Patients who benefit symptomatically from aspiration or drainage of fluid should be offered talc pleurodesis for longer-term benefit.

B - For patients with bone metastasis requiring palliation and for whom standard analgesic treatments are inadequate, single-fraction radiotherapy should be administered.

D - Spinal cord compression is a medical emergency and immediate treatment (within 24 hours), with corticosteroids, radiotherapy and surgery where appropriate, is recommended.

D (GPP) - Patients with spinal cord compression should have an early referral to an oncology physiotherapist and an occupational therapist for assessment, treatment and rehabilitation.

Service Organization

D - All patients with a likely diagnosis of lung cancer should be referred to a member of a lung cancer MDT (usually a chest physician).

D - The care of all patients with a working diagnosis of lung cancer should be discussed at a lung cancer MDT meeting.

A- Early diagnosis clinics should be provided where possible for the investigation of patients with suspected lung cancer, because they are associated with faster diagnosis and less patient anxiety.

D - All cancer units/centres should have one or more trained lung cancer nurse specialists to see patients before and after diagnosis, to provide continuing support, and to facilitate communication between the secondary care team (including the MDT), the patient's GP, the community team and the patient. Their role includes helping patients to access advice and support whenever they need it.

D - Patients who have lung cancer suitable for radical treatment or chemotherapy, or need radiotherapy or ablative treatment for relief of symptoms, should be treated without undue delay, according to the Welsh Assembly Government and Department of Health recommendations (within 31 days of the decision to treat and within 62 days of their urgent referral).

A - Patients who cannot be offered curative treatment, and are candidates for palliative radiotherapy, may either be observed until symptoms arise and then treated, or be treated with palliative radiotherapy immediately.

D (GPP) - When patients finish their treatment a personal follow-up plan should be discussed and agreed with them after discussion with the professionals involved in the patient's care. GPs should be informed of the plan.

A - After completion of their treatment, patients with an expectation of life of more than 3 months should have access to protocol-controlled, nurse-led follow-up.

D - Patients who have had attempted curative surgery for NSCLC or radical radiotherapy should be followed up routinely by a member of the MDT for up to 9 months to check for post-treatment complications. Thoracic imaging should be part of the review.

D - For patients who have had attempted curative surgery for NSCLC, any routine follow-up should not extend beyond 5 years.

D - Patients who have had palliative radiotherapy or chemotherapy should be followed up routinely at 1 month after completion of treatment. A chest X-ray should be part of the review if clinically indicated.

D - Patients with lung cancer -- in particular those with a better prognosis -- should be encouraged to stop smoking.

D (GPP) - The opinions and experiences of lung cancer patients and carers should be collected and used to improve the delivery of lung cancer services. Patients should receive feedback on any action taken as a result of such surveys.

Definitions:

Levels of Evidence for Intervention Studies

1++: High quality meta-analyses, systematic reviews of randomized controlled trials (RCTs), or RCTs with a very low risk of bias

1+: Well-conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias

1 -: Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias

2++: High quality systematic reviews of case-control or cohort studies

High quality case-control or cohort studies with a very low risk of confounding, bias, or chance and a high probability that the relationship is causal

2+: Well-conducted case control or cohort studies with a low risk of confounding, bias, or chance and a moderate probability that the relationship is causal

2-: Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal

3: Non-analytic studies (for example, case reports, case series)

4: Expert opinion

Levels of Evidence for Studies of the Accuracy of Diagnostic Tests

Ia: Systematic review (with homogeneity)* of level-1 studies**

Ib: Level-1 studies**

II: Level-2 studies*** Systematic reviews of level-2 studies

III: Level-3 studies**** Systematic reviews of level-3 studies

IV: Evidence obtained from expert committee reports or opinions and/or clinical experience without explicit critical experience, based on physiology, bench research, or first principles.

*Homogeneity means there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

**Level-1 studies are studies:

- That use a blind comparison of the test with a validated reference standard (gold standard)
- In a sample of patients that reflects the population to whom the test would apply.

***Level-2 studies are studies that have **only one** of the following:

- Narrow population (the sample does not reflect the population to whom the test would apply)
- Use a poor reference standard (defined as that where the 'test' is included in the 'reference', or where the 'testing' affects the 'reference')
- The comparison between the test and reference is not blind
- Case-control studies

****Level-3 studies are studies that have **at least two or three** of the features listed above.

Grading of Recommendations on Interventions

Grade A:

- At least one meta-analysis, systematic review, or randomized control trial (RCT) rated as 1++, and directly applicable to the target population, or
- A systematic review of RCTs or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
- Evidence drawn from a National Institute for Health and Clinical Excellence (NICE) technology appraisal

Grade B:

- A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 1++ or 1+

Grade C:

- A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results, or
- Extrapolated evidence from studies rated as 2++

Grade D:

- Evidence level 3 or 4, or
- Extrapolated evidence from studies rated as 2+, or
- Formal consensus

D (GPP):

A good practice point (GPP) is a recommendation for best practice based on the experience of the Guideline Development Group

Grading of Recommendations on Diagnostic Tests

Grade A (DS): Studies with level of evidence Ia or Ib

Grade B (DS): Studies with level of evidence II

Grade C (DS): Studies with level of evidence III

Grade D (DS): Studies with level of evidence IV

(DS = diagnostic studies)

CLINICAL ALGORITHM(S)

Clinical algorithms are provided in the original guideline document for:

- Diagnosis of Lung Cancer
- Staging of Non-Small Cell Lung Cancer

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

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

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- The use of the most appropriate modalities to diagnose and stage lung cancer, avoiding multiple or unnecessary invasive procedures for the patient
- The use of the most appropriate treatments to enable the best possible outcomes and minimum treatment-related adverse events for patients with lung cancer

POTENTIAL HARMS

- Possible adverse events associated with bronchoscopy include respiratory depression, airway obstruction, pneumonia and possibly death.
- Transbronchial biopsy may result in pneumothorax and haemorrhage (usually mild).
- Transthoracic needle aspiration or biopsy may result in need for insertion of a chest drain, haemoptysis, pneumothorax and possibly death.
- Anterior (parasternal) mediastinotomy may result in morbidity and mortality.
- Thoracoscopy may result in lobar atelectasis, pneumonia and prolonged leak.

- Surgery associated morbidity and mortality
- Radiotherapy can cause pulmonary toxicity leading to early acute pneumonitis (occasionally fatal) or development of chronic pulmonary fibrosis. Oesophagitis is common when the mediastinum is included in the treatment volume. Patients receiving radiotherapy may also experience skin reactions, pericarditis and late oesophageal strictures. A decrease in quality of life may occur.
- Chemotherapy is associated with side effects associated with the various agents and combinations used (see original guideline document for details). Adverse events may include myelotoxicity, haematological toxicity, renal toxicity, nausea and vomiting, alopecia, ototoxicity, constipation, fatigue, peripheral neurotoxicity and infection.

CONTRAINDICATIONS

CONTRAINDICATIONS

- The presence of supraclavicular and contralateral hilar (N3) nodal involvement is regarded by many as a contraindication to radical radiotherapy. Patients with pleural effusion, particularly if cytology positive, are also regarded as ineligible for radical radiotherapy.
- Contraindications to radical radiotherapy include pericardial effusions, cytologically positive pleural effusions and supraclavicular nodes. Contralateral hilar or contralateral mediastinal nodes are relative contraindications for stage III Non-small cell lung cancer) NSCLC.
- Radical radiotherapy is not recommended for those with poor performance status (World Health Organization (WHO) $\geq$2) and for patients with weight loss (a relative contraindication).

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation in the National Health Service (NHS)

Resource Implications

Local health communities should review their existing practice for the diagnosis and management of lung cancer against this guideline. The review should

consider the resources required to implement the recommendations set out in Section 1 of the original guideline document (and in the "Major Recommendations" section of this summary), the people and processes involved and the timeline over which full implementation is envisaged. It is in the interests of patients that the implementation is as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly.

Information on the cost impact of this guideline in England is available on the National Institute for Health and Clinical Excellence (NICE) website and includes a template that local communities can use (www.nice.org.uk/page.aspx?o=244029).

General

This guideline should be used in conjunction with the NICE guidance listed in Section 6 of the short version of the original guideline document.

Audit

A national cancer dataset has been developed by the NHS Information Authority in collaboration with clinicians and the Department of Health. A data subset for lung cancer has been derived by the Intercollegiate Lung Cancer Group to support the National Lung Cancer Data Project (LUCADA), a national ongoing audit programme for lung cancer. Many of the recommendations in this guideline are auditable through this dataset. All English Cancer Networks are being encouraged to take part in this programme which began its national roll-out in July 2004. A copy of the dataset and further details of the LUCADA project can be found at www.icservices.nhs.uk/ncasp/pages/audit_topics/lungcancer/default.asp?om=m1 or www.rcplondon.ac.uk/college/ceeu/ceeu_lung_home.htm.

The audit criteria highlighted in Appendix D of the short version of the original guideline document are based on the recommendations selected as key priorities for implementation. Only two of these highlighted criteria fall within the LUCADA dataset. Audit criteria, exceptions and definitions of terms for those recommendations that are not included in LUCADA are specified.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
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

End of Life Care
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Acute Care. The diagnosis and treatment of lung cancer. London (UK): National Institute for Clinical Excellence (NICE); 2005 Feb. 350 p.

ADAPTATION

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

DATE RELEASED

2005 Feb

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Acute Care - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

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* Shared seat on Guideline Development Group

** Shared seat on Guideline Development Group

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

At each Guideline Development Group (GDG) meeting, all GDG members declared any potential conflict of interests.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format [PDF] format from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies available to order from the National Collaborating Centre for Acute Care (www.rcseng.ac.uk) by email: ncc-ac@rcseng.ac.uk or phone: +44 207869 6630.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- National Collaborating Centre for Acute Care. Lung cancer. The diagnosis and treatment of lung cancer. London (UK): National Institute for Health and Clinical Excellence (NICE); 2005 Feb. 41 p. (Clinical guideline; no. 24). Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Lung cancer. The diagnosis and treatment of lung cancer. Quick reference guide. National Collaborating Centre for Acute Care, 2005 Feb. 11 p. Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Lung cancer--cost impact report and costing template (in English and Welsh) Available from the National Institute for Health and Clinical Excellence (NICE) Web site

Print copies: Available from the National Health Service (NHS) Response Line 0870 1555 455, ref: N0825. 11 Strand, London, WC2N 5HR.

PATIENT RESOURCES

The following is available:

- The diagnosis and treatment of lung cancer. Understanding NICE guidance -- information for people with lung cancer, their families and carers, and the public. National Institute for Health and Clinical Excellence (NICE), 2005 Feb. 39 p.

Electronic copies: Available from the National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: Available from the National Health Service (NHS), 11 Strand, London, WC2N 5HR. Response Line 0870 1555 455, ref N0826.

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 summary was completed by ECRI on May 4, 2005. The information was verified by the guideline developer on September 7, 2005.

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