Lung Cancer

The management guidelines summary for small-cell lung cancers (SCLCs) and non-small-cell lung cancers (NSCLCs) in this article are taken from the guidelines published by the National Institute for Health and Care Excellence (NICE) in April 2011[1]. There are slight variations between national guidelines - eg, Scottish Intercollegiate Guidelines Network (SIGN)[2]. Local agreed guidelines should be followed where applicable.

See also separate Malignant Mesothelioma article - a tumour of mesothelial cells which usually occurs in the pleura but may also occur elsewhere - eg, the peritoneum.

Approximately 95% of all primary lung tumours are bronchial carcinomas. Metastases in the lung are common and typical sites for the primary tumour include the kidney, prostate, breast, bone, gastrointestinal tract, cervix and ovary. Metastases usually develop in the parenchyma and are relatively asymptomatic even when metastases are extensive. Carcinoma of the stomach, pancreas and breast may involve mediastinal glands and spread along the lung lymphatics (lymphangitis carcinomatosa), causing progressive and severe breathlessness.

Primary bronchial cancers are classified as follows:

**SCLCs**
These account for about 15% of cases:

- Also called oat-cell carcinoma, arising from Kulchitsky cells, which are part of the amine precursor uptake and decarboxylation (APUD) endocrine system. APUD cells manufacture polypeptides and amines which act as hormones or neurotransmitters.
- Rapidly growing and highly malignant, they spread early and are almost always inoperable at presentation.
- They respond to chemotherapy but the prognosis is poor.

**NSCLCs**
These account for 85% of cases. The NSCLCs are often grouped together when treatment is being considered. NSCLCs include:

- Squamous (42% of NSCLCs):
  - Most present as obstructive lesions of the bronchus, leading to infection.
  - Local spread is common but widespread metastases occur relatively late.

- Adenocarcinoma (39% of NSCLCs):
  - Arises from mucous cells in the bronchial epithelium.
  - It is the most common bronchial carcinoma associated with asbestos and is more common in non-smokers, compared with other cell types.
  - Invasion of the pleura and the mediastinal lymph nodes is common.
  - It often metastasises to the brain and bones.

- Large-cell (8% of NSCLCs):
  - Are less differentiated forms of squamous cell and adenocarcinomas.
  - Large-cell carcinomas metastasise early.

- Carcinoid tumours (7% of NSCLCs).
- Bronchoalveolar cell (4% of NSCLCs):
  - Occurs either as a peripheral solitary nodule or as diffuse nodular lesions.

**Epidemiology**[1]

There were 46,403 new cases diagnosed in the UK in 2014. 53% were males and 47% were females[3]. More than 35,000 people die from the condition. This is more than colorectal and breast cancer combined. More women now die of lung cancer than breast cancer.

About 90% of lung cancers are caused by smoking. Now that fewer men smoke, lung cancer deaths in men have decreased by more than a quarter in the UK (a 27% reduction between 1971 and 2006). However, the number of women who smoke has risen and deaths from lung cancer in women have increased.

The entity of non-smoking-related NSCLC is becoming increasingly recognised. Passive smoking, occupational exposures, pre-existing lung diseases, diet and oestrogen exposure have all been mooted as possible risk factors[4].

**Risk factors**
Active or passive cigarette smoking is the major risk factor. One study found that cigarette smoking was associated with larger tumours than non-smoking at time of presentation [5].

Increased age.

People with chronic obstructive pulmonary disease. There may be explanations other than smoking (eg, genetic predisposition) for this association [6].

People with a previous history of cancer (especially head and neck) [7].

Industrial dust diseases, asbestos, chromium, arsenic, iron oxides and radiation.

The epidermal growth factor receptor (EGFR) and its ligands are frequently expressed in NSCLC and the EGFR tyrosine kinase (EGFR-TK) inhibitors erlotinib and gefitinib have shown clinical activity in the subgroup of patients with NSCLC who test positive for the EGFR-TK mutation [8].

Presentation [1]

Initial symptoms and signs include:

- Cough.
- Dyspnoea.
- Weight loss.
- Chest pain.
- Haemoptysis.
- Bone pain.
- Finger clubbing.
- Fever.
- Weakness.
- Superior vena cava obstruction.
- Dysphagia.
- Headache.
- Nausea and vomiting.
- Hoarseness (recurrent laryngeal nerve involvement).
- Wheezing and stridor.

Other presentations include recurrent or slowly resolving pneumonia, anorexia, hypertrophic pulmonary osteoarthropathy and supraclavicular or axillary lymphadenopathy.

Chest signs: sometimes no signs; otherwise, consolidation, collapse, pleural effusion.

Metastatic disease: bone tenderness, hepatomegaly, confusion, fits, focal neurological deficit, cerebellar syndrome, proximal myopathy, peripheral neuropathy.

Differential diagnosis

Other causes of a 'coin lesion' (solitary, round, circumscribed shadow in the lung field on CXR):

- Secondary malignancy.
- Arteriovenous malformation.
- Pulmonary hamartoma:
  - Rare, benign tumour.
  - CT scan shows lobulated mass with flecks of calcification.
  - Often excised to exclude malignancy.

- Bronchial adenoma:
  - Rare, slow-growing tumour.
  - 90% are carcinoid tumours; 10% are cylindromas.
  - Treatment is surgery.

- Abscesses.
- Granuloma - eg, tuberculosis.
- Encysted effusion (fluid, blood, pus).
- Gyst.
- Foreign body.
- Skin tumour (eg, seborrhoeic wart).

Referral [9]

Refer urgently (to be seen within two weeks) patients:

- Who have CXR findings suggestive of lung cancer.
- Who are aged over 40 years and have unexplained haemoptysis.

Investigations [1]

- CXR: this may show a peripheral circular opacity, hilar enlargement, consolidation, pleural effusion or bony secondaries.
  - Urgent referral for a CXR (to be performed within two weeks) is indicated for patients over the age of 40 years who have two or more of the following unexplained symptoms or if they have ever smoked and have one of the following symptoms [9]:
- Cough
- Fatigue
- Shortness of breath
- Chest pain
- Weight loss
- Appetite loss

- Urgent CXR (to be performed within two weeks) should also be considered for patients aged over 40 years with any of the following:
  - Persistent or recurrent chest infection.
  - Finger clubbing.
  - Supraclavicular lymphadenopathy or persistent cervical lymphadenopathy.
  - Chest signs consistent with lung cancer.
  - Thrombocytosis.

- Contrast-enhanced chest CT scan:
  - To stage the tumour. The scan should also include the liver and adrenal glands. Chest CT scan should be performed before an intended fibre-optic bronchoscopy or any other biopsy procedure.

- Positron emission tomography (PET)-CT scan:
  - All potentially curable patients should also be offered a PET-CT scan before treatment.
  - This technique involves the use of PET and CT equipment on the same gantry. The images obtained are superimposed and can give a very precise localisation of pathology.

- Bronchoscopy:
  - To establish an histological diagnosis and assess operability.
  - This should be performed on patients with central lesions where nodal staging does not influence treatment.

- Neck ultrasound:
  - If there is a high suspicion of mediastinal malignancy on CT scanning, neck ultrasound should be offered with sampling of visible lymph nodes or non-ultrasound-guided transbronchial needle aspiration (TBNA).
  - If neck ultrasound is negative, non-ultrasound-guided TBNA, endobronchial ultrasound-guided (EBUS) TBNA or endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) should be performed.

- Surgical biopsy:
  - Should be performed for diagnosis where other less invasive methods of biopsy have not been successful or are not possible.
  - Biopsies should be taken from metastases if this can be achieved more easily than from the primary site.

- Percutaneous transthoracic needle biopsy:
  - For diagnosis of peripheral lesions and superficial lymph nodes.
  - Thoracoscopy should be considered for patients with pleural effusions or peripheral lesions where less invasive means have not achieved histological and cytological confirmation of diagnosis [2].

- Anterior mediastinotomy/mediastinoscopy [2]:
  - Should be considered in patients with lung cancer presenting with hilar and mediastinal masses where histological or cytological confirmation has not been achieved by less invasive means.

- An 18F-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.

- Lung function tests.
- Cytology:
  - Sputum and pleural fluid.
  - 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.

- Testing for the EGFR-TK mutation may have important implications in the choice of treatment for patients with NSCLC.

**Investigations for metastases [2]**

**NSCLC**

- All patients with NSCLC who are being considered for radical treatment should have a staging PET-CT scan to detect occult distant metastases.
- Brain:
  - Contrast-enhanced head CT or MRI in asymptomatic patients with clinical stage I-II disease is not recommended.
  - Contrast-enhanced head CT or MRI is warranted in patients with N2 disease who are being considered for curative treatment.
• Bone:
  • Bone scanning with technetium $^{99m}$Tc has a high false positive rate.
  • Compared to conventional isotope bone scanning, FDG PET-CT is more specific and sensitive. If a PET scan is not indicated and symptoms of bone metastases are present, a technetium $^{99m}$Tc nuclear bone scan may be helpful.
  • A positive bone scan should be confirmed by additional studies (eg, X-ray, MRI, biopsy).

• Liver:
  • Ultrasound, contrast-enhanced CT, FDG PET-CT or MRI can be used to characterise most benign focal hepatic abnormalities >10 mm.
  • A definitive confirmation of a liver metastasis can only be made by needle biopsy.

SCLC

• Investigation for distant metastases is recommended when intensive treatment is being considered for patients with SCLC who are considered to be at high risk of having distant metastases.
• Patients with SCLC should be staged by clinical evaluation and contrast-enhanced CT of the chest and abdomen. If the CT does not demonstrate extensive disease and the clinical examination is negative, management should proceed on the assumption of limited stage disease.

Staging and management of non-small-cell lung cancer[1]

Staging

• Follows the 'tumour, node, metastasis' (TNM7) classification[10]:
  • Tumour (T):
    • TX - positive malignant cytology results, no lesion seen.
    • T0 - no evidence of primary tumour.
    • T1 - diameter smaller than, or equal to, 3 cm.
    • T1a - tumour ≤2 cm.
    • T1b - tumour>2 cm and ≤3 cm.
    • T2:
      • Associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung.
      • Tumour with any of the following features of size or extent:
        • Over 3 cm but less than 7 cm in greatest dimension.
        • Involves the main bronchus.
        • Over 2 cm distal to the carina.
      • Invades the visceral pleura.
    • T2a - tumour >3 cm and ≤5 cm.
    • T2b - tumour >5 cm and ≤7 cm.
  • T3:
    • Tumour >7 cm that directly invades any of the following: chest wall (including superior sulcus tumours), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or
    • Tumour in the main bronchus <2 cm distal to the carina but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumour nodule(s) in the same lobe.
  • T4 - invasion of mediastinal organs (eg, the oesophagus, trachea, great vessels, heart), malignant pleural effusion, recurrent laryngeal nerve, or satellite nodule(s) within the primary lobe or separate tumour nodule(s) in different ipsilateral lobe.

• Regional lymph node involvement (N):
  • N0 - no lymph nodes involved.
  • N1 - ipsilateral bronchopulmonary or hilar nodes involved.
  • N2 - ipsilateral mediastinal or subcarinal nodes.
  • N3 - contralateral mediastinal, hilar, any supraclavicular nodes involved.

• Metastatic involvement (M):
  • M0 - no metastases.
  • M1 - metastases present.
  • M1a - separate tumour nodule(s) in contralateral lobe or tumour with malignant pleural (or pericardial) effusion.
  • M1b - distant metastasis.
Stage groupings:
- IA - T1 N0 M0.
- IB - T2 N0 M0.
- IIA - T1 N1 M0.
- IIIB - T2 N1 M0 or T3 N0 M0.
- IIIA - T1-3 N2 M0 or T3 N1 M0.
- IIIB - any T4 or any N3 M0.
- IV - any M1.

Management
- Patients with lung cancer who smoke, in particular those with a better prognosis, should be encouraged to stop smoking. They should be advised that smoking cessation reduces post-surgery lung complications. Surgery should not, however, be postponed until the patient has stopped smoking.
- For patients with NSCLC being considered for curative surgery, a global risk assessment tool (eg, Thoracoscore) should be used to calculate the risk of death. The patient should be advised of this score before being asked to sign the consent form.
- Lung function tests should be performed on all patients pre-surgery.
- Cardiovascular risk should be assessed, especially in patients with a history of cardiovascular comorbidities.
- Surgical resection:
  - The treatment of choice for patients with stage I or stage II disease. Lobar resection is the procedure of choice. Patients with stage I or stage II disease who would not tolerate lobectomy because of comorbid disease or pulmonary compromise, should be considered for limited resection or radical radiotherapy.
  - More extensive surgery (eg, broncho-angioplastic surgery, bilobectomy, pneumonectomy) should only be undertaken if such procedures are necessary to obtain tumour-free margins.
  - All patients undergoing surgical resection should have hilar and mediastinal lymph node sampling to provide accurate pathological staging.
  - In patients with stage IIIA NSCLC, surgery alone is associated with a relatively poor prognosis.
- Radiotherapy:
  - This should be offered to all patients with stage I-III NSCLC who are not suitable for surgery.
  - Radical radiotherapy is indicated for patients with stage I, II or III NSCLC who have good performance status and whose disease can be encompassed in a radiotherapy treatment volume without undue risk of normal tissue damage.
  - All patients should undergo pulmonary function tests (including lung volumes and transfer factor) before having radical radiotherapy.
  - 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.
- Chemotherapy:
  - Chemotherapy should be offered to patients with stage III or IV NSCLC and good performance status, to improve survival, disease control and quality of life.
  - Second-generation chemotherapeutic agents include ifosfamide, vinblastine, vindesine, mitomycin C and platinums (carboplatin and cisplatin). More recently, the third-generation drugs (gemcitabine, paclitaxel, vinorelbine and docetaxel) have been shown to have significant activity against NSCLC, alone or in combination.
  - Patients who are unable to tolerate a platinum combination may be administered docetaxel, paclitaxel or vinorelbine plus a platinum drug. Either carboplatin or cisplatin may be administered in combination.
  - 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.
- Pembrolizumab:
  - Pembrolizumab in combination with cisplatin is recommended as an option for the first-line treatment of patients with locally advanced or metastatic NSCLC only if the histology of the tumour has been confirmed as adenocarcinoma or large-cell carcinoma.
  - Pembrolizumab is recommended as an option for the maintenance treatment of people with locally advanced or metastatic NSCLC other than predominantly squamous cell histology if disease has not progressed immediately following platinum-based chemotherapy in combination with gemcitabine, paclitaxel or docetaxel.
- Erlotinib:
  - Erlotinib is recommended as a possible treatment for people with locally advanced or metastatic NSCLC that has already been treated with non-targeted chemotherapy because of delayed confirmation of EGFR mutation status, if:
    - Their cancer tests positive for the EGFR mutation; or
    - It is not known if the cancer is EGFR mutation positive because of problems with the test; and:
      - The cancer is very likely to be EGFR mutation positive.
  - It responds to the first two cycles of treatment with erlotinib.
- Afatinib:
  - Afatinib is recommended by NICE for the treatment of locally advanced or metastatic NSCLC with activating EGFR mutations, in patients who have not previously been treated with EGFR-TK inhibitor.
- **Crizotinib**[^2,^19]:
  - This is recommended by NICE for the treatment of previously treated anaplastic lymphoma kinase (ALK)-positive advanced NSCLC.

- **Gefitinib**:
  - Gefitinib is recommended as an option for the first-line treatment of people with locally advanced or metastatic NSCLC if they test positive for the EGFR-TK mutation[^20].
  - However, NICE does not recommend the NHS use of gefitinib for the second-line treatment of locally advanced or metastatic NSCLC.

- **Bevacizumab**:
  - Bevacizumab, in combination with platinum-based chemotherapy, is licensed for first-line treatment of unresectable advanced, metastatic or recurrent NSCLC other than predominantly squamous cell histology.
  - However, bevacizumab is currently not recommended by NICE for the treatment of lung cancer.

- **Nintedanib**:
  - Nintedanib is licensed for the treatment of locally advanced, metastatic or locally recurrent non-small cell lung cancer of adenocarcinoma histology after first-line chemotherapy (in combination with docetaxel) initiated under specialist supervision. It is recommended by NICE[^21].

- **Targeted therapy** - this relies on the use of biomarkers to identify specific mutations. Personalised treatments aimed at these mutations can then be developed[^22].

- **Combination therapy**:
  - Postoperative radiotherapy should be considered after incomplete resection of the primary tumour for patients with NSCLC, with the aim of improving local control.
  - Adjuvant chemotherapy should be offered to NSCLC patients who have had a complete resection.
  - Patients with stage III NSCLC, who are not suitable for surgery but are eligible for radical radiotherapy, should be offered sequential chemotherapy and radical radiotherapy.

- **Percutaneous radiofrequency ablation**:
  - Percutaneous radiofrequency ablation may be used in patients with primary or secondary lung cancers. There is a small incidence of pneumothorax, which may have serious implications for patients with already compromised respiratory reserve[^23].

### Staging and management of small-cell lung cancer[^1]

#### Staging

- Staging investigations include serum lactate dehydrogenase, LFTs and serum sodium.
- Should be staged by a contrast-enhanced CT scan of the patient's chest, liver and adrenal glands and by selected imaging of any symptomatic area. A two-stage system of staging is used:
  - **Limited-stage disease** - this includes patients with disease that:
    - Is confined to one hemithorax.
    - Involves ipsilateral hilar lymph nodes.
    - Involves ipsilateral and contralateral supraclavicular lymph nodes.
    - Can be with or without ipsilateral pleural effusions, independent of cytology.
  - **Extensive-stage disease** - disease at sites beyond the definition of limited disease. This includes patients with:
    - Metastatic lesions in the contralateral lung.
    - Distant metastatic involvement (eg, brain, bone, liver or adrenal glands).

#### Management

- Patients with lung cancer, in particular those with a better prognosis, should be encouraged to stop smoking.
- All patients with SCLC should be offered multidrug regimens, because they are more effective and have a lower toxicity than single-agent regimens.
- Patients with limited-stage disease should be offered four to six cycles of cisplatin-based combination chemotherapy (carboplatin in patients with impaired renal function or significant comorbidity)[^22].
- Oral topotecan is recommended as an option only for people with relapsed SCLC for whom re-treatment with the first-line regimen is not considered appropriate and the combination of cyclophosphamide, doxorubicin (formerly known as Adriamycin®) and vincristine (CAV) is contra-indicated[^24].
- 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.
- Patients with limited disease and complete or good partial response after primary treatment should be offered prophylactic cranial irradiation[^25].
- 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.
- Patients with extensive-stage disease should be offered platinum-based combination chemotherapy to a maximum of six cycles.
• As with NSCLC, targeted therapy is also being studied, although phase II and III trials have met with limited success\(^{[28]}\).
• Thoracic radiotherapy after chemotherapy may be beneficial in selected patients.
• Surgery may be an option in patients presenting at an early stage.

Iron deprivation
Research suggests that iron deprivation may have a role to play in the management of lung cancer and indeed other types of cancers. In vitro iron deprivation results in a number of biochemical changes which inhibit cellular proliferation and increase apoptosis. Further studies are required to determine whether this translates into beneficial effects in vivo and whether iron chelation could be considered as a potential adjunct in cancer therapy\(^{[27]}\).
Supportive and palliative care for lung cancer[1]

The following list is a brief outline of certain aspects of palliative care for patients with lung cancer. Guidance is also provided in the British National Formulary[12].

- **Breathlessness:**
  - Strong opiate - eg, morphine or diamorphine.
  - Non-drug interventions based on psychosocial support, breathing control and coping strategies should be considered.

- **Bronchial obstruction:**
  - External beam radiotherapy.
  - Debunking bronchoscopic procedures (for large airway obstruction).
  - Patients with extrinsic compression may be considered for treatment with stents.

- **Pleural effusion:**
  - Pleural aspiration or drainage should be performed.
  - Patients who benefit symptomatically from aspiration or drainage of fluid should be offered talc pleurodesis for longer-term benefit.

- **Haemoptysis if distressing:**
  - Radiotherapy.
  - Debunking bronchoscopic procedures should be considered for the relief of bleeding due to an endobronchial tumour within a large airway.

- **Cough:**
  - Opioids (eg, codeine, morphine).
  - Radiotherapy.

- **Chest pain:**
  - Radiotherapy.

- **Troublesome hoarseness due to recurrent laryngeal nerve palsy:**
  - Refer to an ear, nose and throat specialist for advice.

- **Superior vena cava obstruction:**
  - Chemotherapy and radiotherapy according to the stage of disease and performance status.
  - Stent insertion should be considered for the immediate relief of severe symptoms of superior vena cava obstruction or following failure of earlier treatments[28].

- **Bone pain:**
  - For patients with bone metastasis requiring palliation and who have not been helped by standard analgesic treatments, single-fraction radiotherapy should be considered.

- **Cerebral metastases:**
  - Corticosteroids and radiotherapy should be considered.

- **Spinal cord compression:**
  - This is a medical emergency and immediate treatment (within 24 hours), with corticosteroids, radiotherapy and surgery where appropriate, is recommended.
  - Patients with spinal cord compression should have an early referral to an oncology physiotherapist and an occupational therapist for assessment, treatment and rehabilitation.
Complications[1]

Local
- Recurrent laryngeal palsy, phrenic nerve palsy, Horner's syndrome, Pancoast's syndrome.
- Cardiovascular: superior vena cava obstruction, pericarditis, atrial fibrillation.
- Rib erosion.

Metastatic
- Brain: confusion, fits, local neurological deficit, cerebellar syndrome.
- Bone: bone pain, hypercalcaemia.
- Liver: hepatomegaly.
- Adrenal: Addison's disease.

Non-metastatic[29]
- Endocrine: inappropriate antidiuretic hormone (ADH) secretion, non-metastatic hypercalcaemia, Cushing's syndrome, gynaecomastia, hypoglycaemia, hyperthyroidism.
- Skeletal: hypertrophic pulmonary osteoarthropathy (joint stiffness and severe pain in the wrists and ankles, sometimes with gynaecomastia. This is usually associated with clubbing of the fingers. It may regress after resection of the lung tumour).
- Renal: glomerulonephritis, nephrotic syndrome.
- Collagen/vascular: myositis, vasculitis, systemic lupus erythematosus, endocarditis.
- Cutaneous: acquired hypertrichosis lanuginosa, erythema gyratum repens, erythema multiforme, tylosis, erythroderma, exfoliative dermatitis, acanthosis nigricans, thrombophlebitis migrans, pruritus, urticaria, dermatomyositis.
- Haematological: anaemia, thrombocytosis, thrombocytopenic purpura, disseminated intravascular coagulation.

Prognosis[1]
- The ten-year survival rate for lung cancer in the UK is about 5.5%. The rate is gradually rising but this improvement is comparatively slow compared to other cancers. There is a better survival rate in other European countries and North America. There are variations of outcome within the UK which may partly be explained by variations in the standard of care.
- The seventh revision of the TNM staging system has identified new subgroups which have significantly different prognoses. For example, T1a has a better prognosis than T1b (93% versus 70% five-year survival)[29].
- NSCLC has a much better prognosis than SCLC. 65-70% of patients have disseminated or extensive disease at presentation.
- Changes in smoking habits have resulted in differences in mortality rates between the sexes. Smoking in men has reduced and there has consequently been a reduction in deaths from lung cancer: a 27% reduction between the years 1971 and 2006. Smoking in women has increased, however, resulting in an inevitable rise in lung cancer deaths.
- There is some evidence that patients with NSCLC who stop smoking after diagnosis have a better prognosis.
- Limited evidence suggests that women taking oestrogen-progestogen combinations have a worse prognosis once diagnosed with NSCLC and that anti-oestrogens may have a preventative effect in the development of the disease.
- Some studies suggest that aspirin improves the survival of adenocarcinoma patients (in common with other solid tumours).

Prevention[1]
- Actively discourage smoking and encourage smoking cessation.
- Prevent occupational exposure to carcinogens.
- Lung cancer screening programmes are being instituted in high-risk populations[31].

Further reading & references
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