Diagnosis and Management of Lung cancer

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<table>
<thead>
<tr>
<th>Scotland</th>
<th>Males</th>
<th>Females</th>
</tr>
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<tbody>
<tr>
<td>Rank – Incidence (2013)</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Rank – Mortality (2014)</td>
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<tr>
<td>Percentage frequency of all cancers – incidence (2013)</td>
<td>17.1%</td>
<td>16.0%</td>
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<tr>
<td>Percentage frequency of all cancers – mortality (2014)</td>
<td>26.2%</td>
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<tr>
<td>Number of new cases diagnosed in 2013</td>
<td>2,571</td>
<td>2,553</td>
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<tr>
<td>Number of deaths recorded in 2014</td>
<td>2,119</td>
<td>1,998</td>
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### Summary statistics for lung cancer (ISD)

<table>
<thead>
<tr>
<th>Scotland</th>
<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td>Change in incidence from 2003 to 2013</td>
<td>-15.0%</td>
<td>+13.4%</td>
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<tr>
<td>Change in mortality from 2004 to 2014</td>
<td>-21.4%</td>
<td>+2.0%</td>
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<tr>
<td>1 year relative survival for patients diagnosed between 2007 and 2011</td>
<td>30.0% (↑)</td>
<td>33.0% (↑)</td>
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<td>5 year relative survival for patients diagnosed between 2007 and 2011</td>
<td>8.8% (↑)</td>
<td>10.9% (↑)</td>
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<td>Projected % change between 2008-12 and 2023-27</td>
<td>12.1% (↑)</td>
<td>29.0% (↑)</td>
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Causes of Lung Cancer

- Smoking – 86% of all lung cancers are linked to smoking.
- Exposure to radon gas (particularly in areas where there is a lot of granite)
- Exposure to certain chemicals such as asbestos, fumes, dust
- Family history of lung cancer
- Previous cancer treatment e.g. following radiotherapy for breast cancer or lymphoma
Signs and Symptoms of Lung Cancer

- A cough that lasts more than two or three weeks
- A long-standing cough that gets worse
- Recurrent chest infections
- Haemoptysis
- A pain when breathing or coughing
- Persistent or worsening breathlessness
- Persistent fatigue
- Loss of appetite or unexplained weight loss
- Hoarseness
- Finger clubbing
Reasons for delay in seeking care

- Corner J et al (2006) carried out interviews with patients who had recently been diagnosed with both operable and inoperable lung cancer to study events recalled prior to diagnosis.
- They found that experiences were similar regardless of stage or social background.
- They found six themes which related to experiences of health changes and reasons for delay in seeking help. These were
  - Experiencing uncertainty over what was ‘normal’ and being slow to go to a doctor for help
  - health changes as ‘everyday’ fluctuations of bodily functioning
  - disconnected interpretations of bodily changes
  - the problem of co-morbidity
  - not associating health changes with lung cancer
  - and feeling unworthy of treatment.
Smoking and Lung Cancer

- Cancers are caused by mutations in the DNA of cancer cells
- Typical smoker will acquire one mutation for every 15 cigarettes smoked
- Many of the mutations are repaired but some key genes can be affected which can lead to lung cancer.

(Wellcome Trust Sanger Institute, 2009)
Prevention is better than cure

- The association between lung cancer and smoking is more strongly related to the duration of smoking over time rather than the amount of tobacco smoked per day.

- Peto et al (2000) found that the cumulative risk of death from lung cancer by age 75 was estimated at 16% among current smokers, this increased to 24% for those who smoked at least 25 cigarettes per day.

- Cumulative risk for never smokers was 0.2%
Prevention is better than cure

- Crispo et al (2004) using the same data found that the cumulative risk of lung cancer by age 75 was 11.1, 5.6 and 2.6% among men who stopped smoking at 60, 50 and 40 years respectively.
- They concluded that for people who have been smoking for many years, quitting in middle age avoids most of the subsequent risk of developing lung cancer.
Screening for Lung Cancer

- The National Lung Screening Trial Research Team conducted an American trial comparing annual CT to CXR

- They found that there was a relative reduction in mortality from lung cancer of 20% in those who underwent CT scans compared to CXR
Screening for Lung Cancer

- However, there was a high rate of false positives (96.4% in CT and 94.5% in CXR groups respectively).

- The number needed to be screened by CT to prevent one lung cancer death was 320.
Screening for Lung Cancer

- Currently a lung cancer screening programme going on in Scotland using a blood test, EarlyCDT-Lung.

- Trial will include 12,000 high risk smokers or ex smokers, who are aged between 50 and 75.
Screening for Lung Cancer

- Half of group will have EarlyCDT-Lung test and those who are positive will be followed up with CXR and CT to see if lung cancer present. If no abnormalities they will be offered scans every 6 months for 2 years.

- Other half will have current standard of care.

- Participants will be tracked for 10 years to see if anyone develops cancer.
Smoking cessation

- Undertaking smoking cessation may reduce their risk of postoperative complications following lung resection as well as long term benefits (Theadom and Cropley, 2006).

- Meta analysis, conducted by Parsons et al (2010), has shown that patients with an early stage NSCLC who stop smoking have an increased overall survival and decreased rate of recurrence.

- In patients with SCLC stopping smoking has shown an increased overall survival and reduced rate of second primaries and recurrence.
Electronic cigarettes

- They contain nicotine but no tobacco.
- They deliver nicotine in a vapour rather than in smoke.
  - Current expert evidence suggest that using e-cigarettes are 95% safer than smoking.
  - Can be used for those who are struggling or not keen to stop smoking in partnership with smoking cessation services.
- Need to await more studies on the long-term effects of e-cigarettes.
Types of Lung Cancer

Broken down into 2 main groups

- Non small cell lung cancer
- Small cell lung cancer
Types of Non Small Cell Lung Cancer

- **Adenocarcinoma (35-40%)**
  Develops from the cells which produce mucous in the lining of the airways
  Usually found in the outer part of the lung
  It’s the most common form of lung cancer in women and people who have never smoked.
  It’s the most common type of lung cancer in people less than age 50.

- **Squamous cell Carcinoma (25-30%)**
  Develops in the cells which line the airways
  Often caused by smoking
  Tend to be found in the middle of the lungs, close to a bronchus
  Often invades neighbouring structures
  More common in men and in people over age 65 of both sexes

- **Large cell carcinoma (10-15%)**
  Can start in any part of the lung
  Tends to grow and spread quickly
TNM Classification

- TNM classification is made up of:
  - T descriptor: defines the extent of the primary tumour
  - N descriptor: defines the extent of involvement of regional lymph nodes
  - M descriptor: the extent of spread to distant sites.

Currently using the 7th Edition (2009)
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Stages of Lung Cancer

Images taken from www.researchgate.net
Stages of Lung Cancer

Figure 9. Graphic illustration of stages IIIa and IIIb.
Staging of Lung Cancer

Stage IV
Stage IV includes any T or N

M1a: CNE, N0, M1a

M1a: pleural, M1a: pleural effusion (or pericardial effusion)

M1b: Distant Metastases (common sites depicted)

FIGURE 10. Graphic illustration of stage IV.
Overall survival by clinical stage for the proposed IASLC stage grouping. Reproduced from Goldstraw et al 2007
Multidisciplinary Team Working

Diagnosis

- Radiologist
- Lung Cancer Nurse

Respiratory Physician

Treatment

- Oncologist

Oncologist

Physician

Thoracic Surgeon

Radiologist

Lung Cancer Nurse

Physio

OT

Benefits / HNA

GP

District/community/Tx room nurses

Palliative care

Palliative / Supportive Care
Treatment of Lung Cancer

Treatment decisions are based on a number of factors which include:

- Type of lung cancer
- Stage of lung cancer (size and position of the tumour and whether it has spread out with the lung)
- Performance status/ level of fitness
- Lung function
- Pre-existing co-morbidities

However, it’s important to remember quality of life as well as quantity.
Surgery for NSCLC

- Lung Cancer Quality Performance Indicators (QPI) recommend that 17% of patients with NSCLC should receive surgery.
- In West of Scotland our current surgical rate is 24.2%.
- Lung function and pre-existing co-morbidities may preclude surgery.
- Patients with stage I or II (and sometimes stage IIIA) lung cancer should be considered for surgery where possible.
Surgery for NSCLC

- Lobectomy is the treatment of choice, however, sometimes pneumonectomy is required.
- Mediastinal lymph node sampling should be performed to give accurate staging.
- May be followed by adjuvant chemotherapy.
- Or may be followed by adjuvant radiotherapy if there are not clear margins following resection.
Types of Lung Surgery

- **Wedge Resection** removes a small portion of a lobe.
- **Segment Resection** removes a larger portion of a lobe.
- **Lobectomy** removes an entire lobe.
- **Pneumonectomy** removes the entire lung.

Image taken from www.cts.usc.edu
VATS Surgery for NSCLC

- Video assisted thorascopic surgery (VATS) resection is increasingly being carried out. Minimally invasive technique/keyhole surgery.
- GJNH carried out more VATS resections than thoracotomies last year.
- 2-3 small incisions in the chest (2-4cms long) so smaller surgical wounds.
VATS Surgery for NSCLC

- Only one drain rather than two post surgery.
- Less pain and discomfort.
- Shorter hospital stay (3-5 days) as opposed to average 5-7 days with open thoracotomy.
- Quicker recovery period (2-4 weeks)
Radiotherapy for NSCLC

- Can be used in patients with stage I or II disease who are not suitable for surgery (known as radical radiotherapy)

- May be given after surgery if there are not clear margins around resected tumour

- Stage IIIA or B, either alone or in combination with chemotherapy.

- Palliative radiotherapy for stage 4 NSCLC
  - may consist of 1-2 treatments to palliate symptoms such as cough, haemoptysis, pain (including bone metastases)
  - for brain metastases (usually 5 fractions)
Radiotherapy for NSCLC

- Can be given as one treatment daily for 4 weeks or CHART (Continuous Hyperfractionated Accelerated RadioTherapy) which involves 3 treatments a day for 12 consecutive days.

- Stereotactic radiotherapy (SABRE) for patients with stage 1 peripheral lung tumours who are unsuitable for surgery. Normally given in 5 fractions over 2 weeks. Has shown control rates comparable to surgery.

- High dose palliative radiotherapy. This may be given to people who are not fit for radical treatment or whose treatment fields are too big to give radical RT. May consist of 2 weeks of treatment.
Side-effects of radiotherapy to the chest

- Tiredness/ fatigue
- Oesophagitis (can use analgesia, antacid and oxetacaine)
- Cough
- Skin reaction
- Hair loss (to area being treated)
- Nausea (Particularly if having cranial RT or RT around abdominal area, for example to lower spine).

Later side-effects
- Radiation pneumonitis
- Fibrosis
Side-effects of radiotherapy to the chest

- Patients may find that some of their symptoms such as pain, breathlessness and cough can increase initially following RT as there can be some swelling around the tumour. They should then settle down.
Chemotherapy for NSCLC

- Chemotherapy can be used
  - Neo-adjuvantly prior to surgery
  - Adjuvantly following surgery for stage IB to IIIA
  - Either sequentially or concurrently with radiotherapy for stage III NSCLC
  - Palliatively for stage IV NSCLC
  - Usually given as 4 cycles
Common side effects of chemotherapy

- Low blood cell count
  - White cell count: Increased susceptibility to infection –particularly 7-14 days post chemo
  - Red blood cells: anaemia, tiredness
  - Platelets: bruising, increased risk of bleeding
- Tiredness
Common side effects of chemotherapy

- Sore mouth (mucositis)
- Nausea/ Vomiting
- Constipation/ diarrhoea
- Hair loss
- Peripheral neuropathy
- Sensitivity of the skin to sunlight
Targeted therapies - EGFR

- Molecular testing for predictive biomarkers in NSCLC is becoming a standard of care.

- For all non-squamous NSCLC we are currently testing for EGFR mutation and ALK gene rearrangement.

- Patients usually stay on treatment until there is disease progression or need to discontinue due to side effects.
Targeted therapies - EGFR

- Epidermal Growth Factor Receptor (EGFR) Antagonists
  - When growth factors attach to the receptors, a protein called tyrosine kinase (TK) triggers chemical signals which in turn cause the cell to grow and divide
  - Attach to EGF receptors and prevent the receptor from being activated
EGFR signal

EGFR signals tell cancer cells to grow and multiply out of control.

Tarceva can slow or block these signals. This may cause cancer cells to die. It also affects healthy cells.
Targeted therapies

- EGFR mutation – first line erlotinib or afatinib

Tarceva (Erlotinib) is a TK inhibitor which attaches to the TK protein and stops the signals from being released:
- given as a tablet
- can be given first line in patients who are EGFR receptor positive
- can be given as 2\textsuperscript{nd} or 3\textsuperscript{rd} line treatment
- side effects generally mild and include diarrhoea, nausea, rash and tiredness
Approx 5% of NSCLC tumours have a rearrangement in the ALK gene. The \( ALK \) gene rearrangement produces an abnormal ALK protein that causes the cells to grow and spread. Drugs are used to target the abnormal ALK protein,

ALK rearrangements are more commonly found in adenocarcinomas; patients who are EGFR receptor negative; non smokers and tend to be found in a younger sub group of patients.
Targeted therapies

- ALK positive = first line crizotinib, second line ceritinib.

Crizotinib
- Given in tablet form
- Common side-effects include
  - Nausea and vomiting
  - Diarrhoea
  - Constipation
  - Fatigue
  - Changes in vision.
Targeted therapies

Other targeted therapies that are available now or in the future

- osimertinib (currently only available through early access scheme)
- 2\textsuperscript{nd} line metastatic non-squamous can now get docetaxel with nintedanib
- 2\textsuperscript{nd}/3\textsuperscript{rd} line NSCLC – immunotherapy (mainly nivolumab) is licenced but not smc/nice approved so not available in NHS.
Endobronchial procedures

- Cryotherapy – can be used to treat endobronchial obstruction and symptoms such as cough, dyspnoea and haemoptysis.

- Uses extreme cold to destroy tissue. Cryoprobe is inserted through a bronchoscope to reach the tumour. After a period of freezing, the tumour is allowed to thaw until the probe separates from the tissue. The freeze/thaw cycle may be repeated two to three times in the same place. The probe is then moved to an adjacent area and the process repeated until the whole tumour has been treated. Any resulting necrotic tumour material is then removed with forceps or the cryoprobe. Further necrotic-appearing material may be coughed out 24 to 48 hours later (NICE, 2005).
Endobronchial procedures

- Stenting – can be used in event of extrinsic obstruction of airways by tumour or when there is a broncho-oesophageal or tracho-oesophageal fistula.
- Can be done in conjunction with respiratory physician and interventional radiologist or within the surgical setting.
- Can provide almost immediate relief of symptoms.
**Summary of Treatment Options for NSCLC**

### Stage I
- Lobectomy or segment/wedge resection
- Curative radiotherapy if surgery is contraindicated
- Adjuvant radiotherapy

### Stage II
- Lobectomy, pneumonectomy, segment/wedge resection as appropriate
- Curative radiotherapy if surgery contraindicated
- Adjuvant chemotherapy
- Adjuvant radiotherapy

### Stage IIIA
- Surgery alone
- Radiotherapy alone
- Chemotherapy + radiotherapy
- Post-operative radiotherapy

### Stage IIIB
- Chemotherapy + radiotherapy
- Chemotherapy alone (pall)
- Radiotherapy alone (pall or HD pall)

### Stage IV
- Chemotherapy (platinum based), modest survival benefits
- New chemotherapy agents
- Targeted therapies
- External beam radiotherapy (palliative relief)
- Endobronchial treatment such as laser or cryo.therapy for obstruction
- Radiofrequency ablation
- Best supportive care
Small Cell Lung Cancer

- Approximately 15% of all lung cancers
- Occurs almost exclusively in smokers and is more prevalent in women than men
- Lesions most commonly originate in central part of chest
- Tendency to disseminate early
Small Cell Lung Cancer

- Surgery usually not appropriate (can be considered for patients with early stage disease)
  - Adjuvant chemotherapy should be considered for these patients
- Initially chemosensitive, and responds quickly but also becomes resistant and recurs/progresses rapidly
- Untreated extensive SCLC progresses rapidly with median survival measured in weeks.
Chemotherapy regimes used for SCLC

- Commonly used regimens
  - Cisplatin or carboplatin/etoposide (PE)
  - cyclophosphamide/doxorubicin/vincristine (CAV)

- Carboplatin/ etoposide has become standard for first line treatment – less toxicity than cisplatin/ etoposide and easier to give in outpatient setting.
Radiotherapy for Small Cell Lung Cancer

- Prophylactic Cranial Radiotherapy (PCI) has been shown to reduce the rate of brain metastases and gives a survival benefit.

- Should be considered in both patients with limited and extensive disease who have had response to systemic treatment.
Radiotherapy for Small Cell Lung Cancer

- Consolidation radiotherapy to the chest can be given in patients with limited disease who have responded to chemotherapy.

- Radiotherapy and chemotherapy can also be given concurrently to patients with limited disease in chest who are fit but is not done as commonly.

- Radiotherapy can be given to palliate symptoms also.
Treatment of SCLC

Confined to the chest (Limited disease)
- Platinum based combination chemotherapy (usually combined with Etoposide)
- Consolidation radiotherapy
- Prophylactic Cranial Irradiation (PCI) for those who have shown a response to treatment

Stage IV / metastatic disease (Extensive disease)
- Platinum based combination chemotherapy (usually combined with Etoposide)
- PCI (for those who have shown response to chemotherapy)
Palliative care

- May start from diagnosis (particularly if incurable disease at diagnosis)
- Symptoms to palliate
  - Breathlessness
  - Pain
  - Cough
  - Poor appetite
  - Psychological symptoms such as depression and anxiety
Breathlessness

- Need to get a good history and examination
  - history can establish co morbidities, could breathlessness be related to COPD, CCF?
  - clinical examination could show signs of infection, anaemia, effusion, hypoxia, bronchospasm
Treatment of breathlessness

Need to treat any underlying cause of breathlessness such as:

- pleural effusion,
- pulmonary embolism,
- infection,
- Anaemia
- Large airways obstruction,
- Superior Vena Cava Obstruction (SVCO)
- Lymphangitis carcinomatosa,
- Anxiety
Pharmacological management

- Oxygen – should only be used in patients who have low oxygen levels.
- Opioids
- Benzodiazepines
- Nebulised saline
- Corticosteroids
- Bronchodilators
Non-pharmacological management

- breathing exercises, may involve input of physio or OT
- advice regarding pacing and planning activities
- relaxation techniques
- positioning: positioning in bed (upright), lying with good lung down can improve ventilation perfusion ratio and therefore oxygenation
- Use of a fan or opening a window
- Complimentary therapies such as acupuncture may be of use
Management of Pleural Effusions

- Can perform a therapeutic aspirate to draw a small amount of fluid off and provide symptomatic relief.

- Medical or surgical pleurodesis
  - Talc is the preferred choice of agent
  - Need almost complete drainage of fluid
  - Talc irritates the two linings of the lung and hopefully allows them to stick together and reduce the risk of recurrence of pleural effusion
Management of Pleural Effusions

- Tunnelled pleural catheters can be considered in patients who experience recurrent pleural effusions or whose effusions are unable to be drained to dryness.

- They allow patients to be managed at home and prevent re-admission. About 25% of effusions will drain to dryness following pleural catheter insertion.
Psychological Implications of Lung Cancer

- Lung cancer patients have been shown to have one of the highest rates of distress (43%) when compared to other cancer groups including breast cancer and colorectal cancer.

(Zabora J, Brintzenhofeszoc K, Curbow B, Hooker C and Piantadosi S, 2001)
Holistic Care of Lung Cancer Patients

Murray SA et al (2007) carried out a study looking at the psychological, social, and spiritual needs of people with lung cancer during their last year of life. They found that:

- Social trajectory mirrored physical decline
- However, psychological and spiritual well-being decreased together at four key transitions
  - Diagnosis
  - Discharge after treatment
  - Disease progression
  - Terminal stage
Conclusions

- Need to work towards diagnosing lung cancer earlier through:
  - wider knowledge of signs and symptoms of lung cancer
  - Continuing to look at ways to screen for lung cancer in high risk groups

- Treatment opportunities have increased for lung cancer patients and targeted therapies may be the future of lung cancer treatment.

- It’s important to look past the physical aspects of lung cancer in order to see the whole picture.