Early detection of lung cancer in primary care

Lung cancer is one of the most common cancers in New Zealand and the leading cause of cancer death. By the time of diagnosis, most people already have advanced disease, when there is little or no chance of cure. Increasing the early detection of lung cancer in high-risk symptomatic people is therefore key to improving survival outcomes.

KEY PRACTICE POINTS:

- Lung cancer accounts for the most cancer-related deaths in New Zealand; mortality rates are high compared to countries with similar healthcare systems
- Lung cancer incidence and mortality rates in Māori and Pacific peoples are two to three times higher than in Europeans/Others
- Early detection of lung cancer increases the chance of survival, however, many people present late when the disease is already at an advanced stage. Contributing factors include the subtlety of symptoms, difficulties accessing care because of cost, location or other systemic barriers, and psychological factors such as denial or fear.
- Clinical barriers to early detection include the lack of specific symptoms, attributing symptoms to another respiratory condition or cause (e.g. smoking), and discontinuities in care
- People at high risk of lung cancer include those with a current or previous history of smoking, asbestos exposure, pre-existing lung disease, personal history of any cancer or family history of lung cancer. All people at high risk should undergo a respiratory assessment annually to determine if symptoms are present (see below). Most lung cancers are diagnosed in people aged > 40 years.
- Key symptoms and signs that may be suggestive of early-stage lung cancer, particularly in those with known risk factors, include unexplained persistent (> 3 weeks) cough (new or changed), haemoptysis, chest or shoulder pain, unresolved or recurrent chest infection, breathlessness, hoarseness and weight loss
- Refer people aged 40 years and over with symptoms or signs of lung cancer for urgent chest x-ray (preferably same day, if available); x-ray should be completed, reviewed and reported within one week of referral

Lung cancer is the leading cause of cancer death in New Zealand

Lung cancer is one of the most common cancers in New Zealand and accounts for the most cancer-related deaths.[1] In 2017, there were 2,232 lung cancer* registrations and 1,779 lung cancer deaths, equating to nearly 20% of all cancer deaths.[2,3] Lung cancer mortality rates in New Zealand are high compared to other countries with similar healthcare systems. A comparison of five-year survival rates (2010–2014) between seven high-income countries† found that New Zealand had the second lowest lung cancer survival rate (16%), ahead of only the United Kingdom (15%); the highest survival rates were in Canada (22%) and Australia (21%).[4] Various factors are likely to explain this finding, including late presentation and diagnosis and lack of access to funded treatments.

* Includes malignancy of the trachea, bronchus and lung (ICD-10 codes C33–C34)

† Australia, Canada, Denmark, Ireland, New Zealand, Norway and the United Kingdom

Early detection is key to increasing lung cancer survival rates

The stage at diagnosis is a major determinant of lung cancer prognosis, i.e. the earlier the stage the greater the chance of curative treatment. A study of people in the New Zealand Midland Cancer Network region who were diagnosed with early-stage lung cancer (stage I and II – see "Types and stages of lung cancer" for definitions) between 2011–2018 found a five-year survival rate of 70% in those who underwent curative-intent treatment – mainly surgery, but increasingly with stereotactic ablative body radiotherapy.[5] However, most people have advanced disease at diagnosis (see: "Factors contributing to the late presentation and detection of lung cancer"). Another study in the Midland Cancer Network region found that only 17% of people were diagnosed with early-stage lung cancer; 61% were diagnosed with advanced-stage (stage IV) cancer.[6] The one-year survival rate in people diagnosed with advanced lung cancer is typically < 20%.[7]

Types and stages of lung cancer

There are two main classifications of lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC is the most common type of lung cancer; 89% of people in New Zealand diagnosed with lung cancer between 2008 and 2012 had NSCLC.[1] SCLC tends to metastasise earlier, is more aggressive and harder to treat than NSCLC.[6] SCLC is more common in Māori than non-Māori, even after controlling for smoking status;[6] the reason for this is not known, but may involve genetic factors.

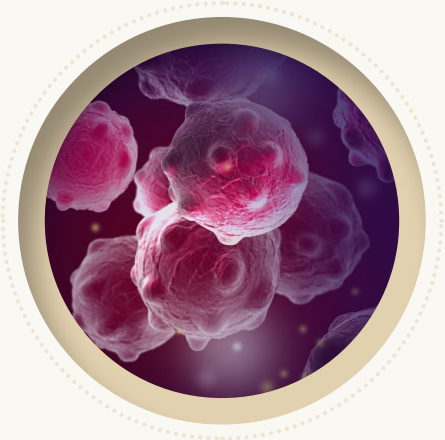
Lung cancer, as with many other cancers, is typically staged using the TNM system, which describes the primary tumour (T), spread to nearby lymph nodes (N) and metastasis (M). The overall stage is then determined based on the TMN characteristics.

The stages of NSCLC are:[8]

- **Stage 0:** The cancer is small in size and has not spread into deeper lung tissues or outside the lungs (also known as carcinoma in situ).
- **Stage I:** Cancer may be present in the surrounding lung tissues, but the lymph nodes remain unaffected.
- **Stage II:** Cancer may have spread to nearby lymph nodes or into the chest wall.
- **Stage III:** Cancer has spread from the lungs to the lymph nodes or to nearby structures and organs, such as the heart, trachea and oesophagus.
- **Stage IV:** Cancer has metastasised to distant lymph nodes, structures or organs not near the lung.

The stages of SCLC are:[9]

- **Limited (equivalent to stages 0–III):** Cancer is only on one side of the chest.
- **Extensive (equivalent to stage IV):** Cancer has spread widely throughout the lung, to the other lung, to lymph nodes on the other side of the chest, or to other parts of the body.



Factors contributing to the late presentation and detection of lung cancer

Illness presentation

Early-stage lung cancer can easily be missed as people are often asymptomatic and when symptoms do develop they are typically non-specific, commonly encountered in primary care, e.g. cough, chest pain, breathlessness, and usually have a non-malignant cause.[12]

N.B. SCLC can present differently to NSCLC (see "Types and stages of lung cancer"); the duration of symptoms is often shorter as SCLC is more aggressive.

Concurrent chronic respiratory symptoms

People with lung cancer often have a history of chronic respiratory symptoms or disease, particularly those who smoke[12] Patients and clinicians may have difficulty identifying changes in chronic symptoms and may be more likely to attribute changes to their co-existing respiratory condition and/or to smoking, rather than potential lung cancer.[12] However, chronic respiratory disease is a risk factor for lung cancer, even after controlling for smoking history.[13] Clinicians should therefore have a low threshold for investigating lung cancer in patients who have persistent symptoms, including those with COPD (see: "Assessing people with symptoms and signs of lung cancer").

Psychological factors

Denial, fear, shame and nihilism (belief that if lung cancer is diagnosed it cannot be treated) are common psychological factors that may contribute to people delaying their presentation to primary care or other healthcare service.[12] Public awareness of the causal link between smoking and lung cancer may lead some people to feel embarrassed, ashamed, or think that they are undeserving of or unable to access treatment. Incorporating positive messaging about the benefits of early detection, rather than focusing on blame due to smoking, may help to encourage people who have risk factors for lung cancer to present earlier.

What can primary care do to improve early detection rates?

Increasing early detection is critical to improving lung cancer survival rates, and primary care has an essential role in achieving this outcome by:

- Encouraging people not to start smoking and supporting smoking cessation
- Considering lung cancer as part of the differential diagnosis in patients with symptoms that could be indicative of cancer
- Identifying and assessing people with symptoms and signs of lung cancer and ensuring prompt referral and follow up for chest x-ray and secondary care assessment, as appropriate
- Identifying and assessing people at high risk of lung cancer, and providing advice about when to seek medical attention if they become symptomatic in a non-judgemental way that focuses on the benefits of early detection (see: "Factors contributing to the late presentation and detection of lung cancer")

N.B. A lung cancer screening pilot study including high-risk Māori patients from up to 50 general practices across the Auckland and Waitematā DHBs has been planned.[10] A recent study showed that biennial lung cancer screening with low-dose CT is likely to be cost-effective, improve total population health and reduce health inequities in New Zealand.[11]

Lifestyle, environmental, occupational and personal factors contributing to lung cancer risk

There are a range of factors that increase a person's risk of developing lung cancer (Table 1); those considered at highest risk are people with:[14]

- A current or previous history of smoking
- A history of exposure to asbestos
- Pre-existing lung disease, particularly chronic obstructive pulmonary disease (COPD) or interstitial lung disease
- A personal history of any cancer
- A family history of lung cancer

The incidence of non-smoking-related lung cancer is increasing

The incidence of lung cancer among people who have never smoked is increasing worldwide, particularly in females and people of East Asian ethnicity.[14] The cause of non-smoking-related lung cancer is not always known; genetic susceptibility and/or current or past exposure to environmental or occupational pollutants may explain this trend.[23] People with non-smoking-related lung cancer tend to be significantly younger, have a better prognosis and respond to treatment better than people with smoking-related lung cancer.[23]

Table 1. Risk factors for developing lung cancers[14]

Category	Risk factor	Comments
Lifestyle	Current or previous history of smoking	The major modifiable risk factor for lung cancer; approximately 90% of cases in males and 65% of cases in females are attributed to smoking[15]
Environmental or occupational	Passive smoking	Exposure to passive smoke is estimated to increase the risk of lung cancer by approximately 25%[16]
	Occupational exposure to known carcinogens, e.g. asbestos, diesel exhaust, silica, radon	Asbestos exposure can cause mesothelioma, a peripheral tumour that can be easily missed on chest x-ray if at an early stage Radon exposure in New Zealand is low as soils only contain trace amounts of uranium and radium (the sources of radon).[17] A 2016 survey of indoor radon concentrations in New Zealand buildings (mainly private dwellings/houses in the main centres) identified no radon affected areas that warrant specific monitoring.[18] Underground miners may be exposed to higher concentrations of radon; WorkSafe has guidance outlining ventilation requirements and mine operators are responsible for ensuring monitoring arrangements are in place for detecting radon.[19]
	Air pollution	In general, New Zealand has good air quality in most places at most times of the year.[20] During autumn and winter, emissions from home heating can raise particulate matter to levels above recommended limits, especially when environmental and geographical conditions contribute to build up.[20] However, the extent to which this contributes to lung cancer incidence is not known. A cohort study of people living in urban centres in New Zealand investigating the association between air pollution and mortality found a positive association between estimated long-term exposure to air pollution and lung cancer mortality, i.e. the risk of mortality in people with lung cancer was higher in those exposed to air pollution.[21]
Personal	Increasing age	Lung cancer is rare in people aged < 40 years and is most commonly diagnosed in people aged ≥ 60 years.[6] East Asian ethnicity, female sex and family history are risk factors for a lung cancer diagnosis in people aged < 40 years.
	Family or personal history of lung cancer; personal history of other cancer, e.g. head and neck, bladder	Lung cancer is a common second cancer among people who have survived a first cancer[22]
	Pre-existing lung disease, e.g. COPD, interstitial lung disease, tuberculosis	Cancer risk is likely related to the increased lung inflammation associated with these conditions[13]
	Māori or Pacific ethnicity	Lung cancer incidence rates are two to three times higher in Māori and Pacific peoples than other ethnic groups (see: "Lung cancer incidence and mortality rates are higher in Māori and Pacific peoples")

Lung cancer incidence and mortality rates are higher in Māori and Pacific peoples

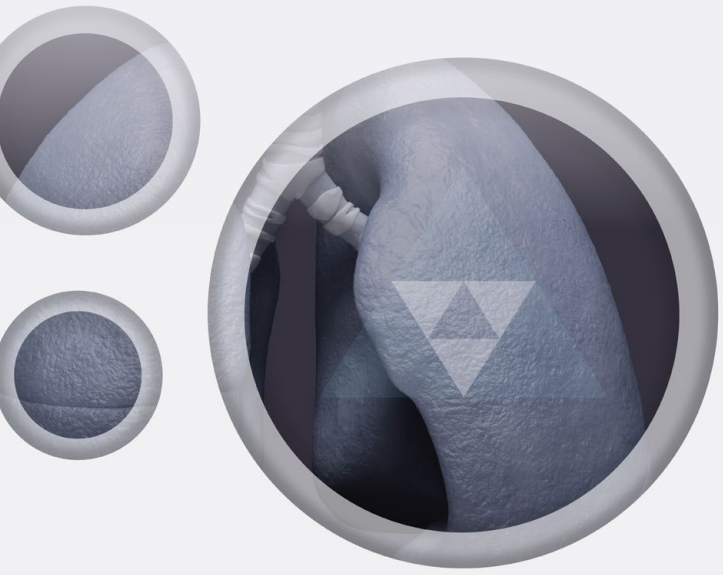
Māori have higher rates of lung cancer at an earlier age than non-Māori.[1] In 2017, the incidence and mortality rates were 3.7 and 3.4 times higher, respectively, in Māori than non-Māori.[2, 3] Lung cancer incidence is higher in Māori females than males, however, the mortality rate is similar between the sexes.[2, 3]

Pacific males are also disproportionately affected by lung cancer. The incidence rate between 2006 and 2011 was nearly two times higher in Pacific males than European/Others and mortality rate was nearly 2.5 times higher.[24] Neither the incidence nor mortality rates for lung cancer were significantly different between Pacific females and European/Others.[24]

High rates of smoking among Māori and Pacific peoples is an important contributing factor to the increased incidence of lung cancer in these groups (see: "Continue to encourage and support smoking cessation"). The 2019/20 New Zealand Health Survey* found that 31% of Māori aged 15 years and older reported current† tobacco smoking, with higher rates in females (35%) than males (27%).[25] Among Pacific peoples, 22% reported current tobacco smoking, with higher rates in males (27%) than females (19%).[25] Smoking rates in Europeans were nearly three-fold lower than Māori and two-fold lower than Pacific peoples.[25] Other contributing factors include higher rates of COPD and reduced healthcare access and continuity of care in these ethnic groups.[26]

* Due to the COVID-19 pandemic, data were collected for three-quarters of the survey year only

† Defined as people who smoke at least monthly and have smoked more than 100 cigarettes in their lifetime



Assessing people with symptoms and signs of lung cancer

The symptoms or signs of lung cancer can be variable and non-specific; they may include:[14, 15, 27]

- Haemoptysis
- Cough (new or changed; may be dry or productive)
- Shortness of breath
- Chest or shoulder pain
- Hoarse voice – due to laryngeal nerve compression
- Fatigue
- Weight loss > 10%
- Abnormal chest signs
- Unresolved chest infection
- Pleural effusion
- Thrombocytosis
- Venous thromboembolism
- Finger clubbing
- Symptoms or signs of metastatic lung cancer, such as in brain, bone, liver or skin (e.g. subcutaneous nodules)
- Cervical or persistent supraclavicular lymphadenopathy
- Superior vena cava syndrome
- Horner syndrome
- Paraneoplastic syndromes

Many of these symptoms or signs will have a cause other than lung cancer. However, due to the benefits of early detection, lung cancer should always be considered in patients who have any of the above symptoms or signs that are unexplained and/or persistent (lasting > 3 weeks*).[14] Even if there is a likely explanation for the patient's symptoms, e.g. recent upper respiratory tract infection, consider whether investigation with chest x-ray is indicated based on risk factors for lung cancer. If immediate chest x-ray is not necessary, arrange a follow-up appointment within an appropriate timeframe to check for symptom resolution; cough in particular can persist for longer than three weeks following a viral respiratory tract infection.

* A shorter timeframe may be appropriate for people with known risk factors or those presenting with multiple symptoms or signs[15]

Immediate referral to the emergency department is indicated for people with:[14, 15]

- Massive haemoptysis
- Signs of airway obstruction, e.g. stridor or respiratory distress
- Signs of superior vena cava obstruction, e.g. dilated veins in neck or over chest, swollen face or head, redness of face
- Symptoms or signs of spinal cord compression

Clinical assessment of patients with suspected lung cancer

The assessment of patients with symptoms or signs suggestive of lung cancer should include:

- A comprehensive history of the symptoms, i.e. onset, duration, frequency, changes from any concurrent respiratory symptoms, change in appetite or weight loss
- Documentation of the patient's personal history of smoking, environmental or occupational exposures to known carcinogens, personal or family history of lung or other cancer
- Physical examination that includes:
  - General appearance and basic observations, e.g. weight, breathlessness at rest or with mild exertion, heart rate, blood pressure, oxygen saturation
  - Respiratory assessment that includes:
    - Inspection – respiratory rate, pattern, effort of breathing, tracheal deviation, peripheral features, e.g. finger clubbing, evidence of superior vena cava obstruction
    - Palpation – chest expansion, chest wall tenderness, tactile fremitus, lymphadenopathy
    - Percussion – including assessment of the diaphragm, presence of localised dullness or effusion
    - Auscultation
  - Abdominal palpation, including assessment of liver size
  - Neurological examination if history suggests spinal cord compression or brain metastases
- Request for laboratory tests:
  - Full blood count
  - Electrolytes and creatinine
  - Calcium – hypercalcaemia is associated with advanced lung cancer
  - Liver function tests
  - Coagulation studies – lung (and other) cancer is associated with hypercoagulation; cancer cells may release substances that directly activate the coagulation cascade, activate endothelial cells and platelets to enhance clotting activation[28]
- Referral for investigations:
  - Urgent chest x-ray – see below
  - Sputum cytology, particularly if haemoptysis is present
  - Spirometry, if available – to detect a restrictive rather than obstructive respiratory pattern

Follow up for patients referred for chest x-ray

Chest x-ray is the first-line investigation for people with suspected lung cancer. Same day access is preferable, but service availability varies by DHB. Some regions have providers that offer "walk in" clinics where patients can access same-day x-ray services following referral, without a prior appointment. This allows greater flexibility and reduces barriers to timely investigation. If same day access is unavailable, chest x-ray should ideally be completed, reported and reviewed within one week of the referral.[15] Ensure that it is clearly documented and communicated who is taking responsibility for following up the results and informing the patient of the outcome, e.g. if the patient has presented at an after-hours clinic.

A repeat chest x-ray after six weeks may be indicated for some patients

If consolidation is found on chest x-ray, repeat after six weeks to confirm that this has resolved.[14] Pneumonia and episodes of atelectasis can occur due to airway blockage by a tumour, which may then not be immediately detected due to the associated inflammatory processes.[29] Ensure that patients who require a repeat chest x-ray are followed up, and that the results are communicated to them. Slowly resolving or unresolved consolidation can be suggestive of lung cancer and patients should be referred for assessment by a respiratory physician.[14]

Consider a repeat chest x-ray or referral for high-risk patients who have persistent symptoms or signs for more than six weeks even if the initial chest x-ray was normal, as this may not exclude lung cancer.[14] Some analyses indicate that up to 25% of lung cancers may be not be identified on chest x-ray.[15]

When to refer patients with suspected lung cancer

Urgent referral for assessment by a respiratory physician is indicated for:[14, 15]

- People with chest x-ray or other imaging* suggestive or suspicious of lung cancer, including new pleural effusion, pleural mass, mass elsewhere in the lung fields/ mediastinum, or slowly resolving consolidation
- Persistent or unexplained haemoptysis in high-risk individuals aged over 40 years
- People with a high clinical suspicion of cancer (i.e. symptoms and signs of lung cancer and in a high-risk group), despite normal chest x-ray

* In some DHBs, general practitioners may be able to refer directly for chest CT, with or without advice from a respiratory physician or radiologist

Flag the referral as 'high suspicion of lung cancer'.

Managing people at high risk of lung cancer

Identifying patients who are at high risk* of lung cancer and ensuring that they are asked regularly about their respiratory health and undergo an annual respiratory assessment increases the likelihood of detecting potential lung cancer early. This assessment should include referral for chest x-ray† if they have any symptoms suggestive of lung cancer and:[30]

- The patient has not had a chest x-ray in the previous 12 months

OR

- The patient presents with new symptoms

N.B. There may be clinical scenarios where chest x-ray is indicated even though the patient has had one in the previous 12 months.

* Defined as current or previous history of smoking, history of exposure to asbestos, pre-existing lung disease, personal history of any cancer or family history of lung cancer[14]

† While it is acknowledged that this approach is likely to increase demand on health system resources, investigating and treating advanced cancer is also associated with significant burden, both in terms of health system resource utilisation and the socioeconomic costs to the community. Furthermore, expert opinion is that community-referred chest x-ray is currently underutilised in many DHBs.

Discuss the symptoms and signs of lung cancer with people who are at high risk and encourage them to seek medical advice if they develop these or become worried about their health. Emphasise that when detected early, lung cancer can be cured.

Continue to encourage and support smoking cessation

Prevention is ultimately the best strategy to reduce lung cancer rates. Tobacco smoking increases the risk of lung cancer by 20– to 50–fold, with duration of smoking being the strongest determinant of lung cancer risk.[31] The risk decreases within five years of stopping smoking, but is never completely reversed.[31, 32] After 25 years since stopping smoking, the risk of lung cancer is still three times higher than people who have never smoked.[31, 32] Exposure to passive smoke is also associated with an increased risk of lung cancer, with the excess risk estimated to be 20–30% for a non-smoking partner of someone who smokes.[31] The long-term health effects of using electronic cigarettes/vapes in terms of lung cancer risk is not yet known. Data from mice shows the development of lung adenocarcinoma in those exposed to electronic cigarette smoke.[33]

Cannabis smoke also contains carcinogens, however, the association between cannabis smoking and lung cancer incidence is less well understood – the available data are of poor quality and inconclusive.[34] Tobacco smoking among people who smoke cannabis is a major confounding factor, as is the small number of heavy, chronic cannabis users who have been studied.[34]

Ensure that smoking status is regularly updated in the clinical notes of all adolescent and adult patients, and encourage and support smoking cessation in those who currently smoke. The ABC model can be used as a guide:

- **Ask** about and document the smoking status of every patient, including use of e-cigarettes and exposure to passive smoking
- Give **Brief advice** to stop to every patient who smokes
- Strongly encourage every person who smokes to use **Cessation support** and offer help accessing this. A combination of behavioural support and smoking cessation medicine works best.

 For further information on smoking cessation, see: **www.bpac.org.nz/BPJ/2015/October/smoking.aspx**

 A smoking cessation clinical audit is available here: **www.bpac.org.nz/Audits/encouraging-smoking-cessation-2019.aspx**

 For further information on vaping, see: **https://bpac.org.nz/2018/vaping.aspx**

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