

Smoking related cancer MORBIDITY & MORTALITY

Smoking contributes to approximately one in three cancer deaths

Smoking is a significant risk factor for the following cancers:

- Lung
- Head and neck: lip, oral cavity, pharynx and larynx
- Upper GI tract: oesophagus, stomach and pancreas
- Renal tract: bladder and kidney

It is also a risk factor for cancer of the cervix and vulva, uterus and bowel and acute myeloid leukemia.¹

Alcohol appears to potentiate the carcinogenic effect of tobacco, significantly increasing the risks of cancer of the head and neck, stomach, liver and pancreas.

Overall, cigarette smoking contributes to approximately one in three cancer deaths.

Any exposure to tobacco increases the risk of cancer

At an individual level, the risk of developing cancer is related to the life-time exposure to tobacco, the quantity smoked each day, the total number of years smoked and the age that smoking started.² Of all these factors, the length of time that someone smokes seems to be the most significant. For example in people who have smoked for 45 years the risk of lung cancer is 100 times greater than for individuals who have been smoking for 15 years even if the amount smoked each day is less.³

There is no safe level of tobacco exposure. There is measureable risk of cancer with low levels of smoking,^{4,5} occasional smoking,⁶ low tar cigarette smoking and passive smoking.^{7,8}

Stopping smoking reduces cancer risk

Stopping smoking reduces the risk of smoking-related cancers. This effect is most pronounced at younger ages but stopping smoking at any age confers benefit. People who stop smoking at age 30 years reduce their risk to almost that of non-smokers, those at age 50 years can halve the excess risk of cancer,⁹ and mortality is even reduced in people who stop smoking in their seventies.¹⁰

The effect of stopping smoking varies depending on the cancer:¹¹

- The risk of lung cancer halves in about ten years
- The risk of oral and laryngeal cancer takes at least 20 years after stopping to reduce to that of non-smoker
- The risk of bladder cancer takes at least 25 years after stopping to reduce to that of non-smoker

It remains controversial as to whether there is any real benefit from cutting down the number of cigarettes smoked each day.¹² However this may be a strategy for those unable to quit completely.¹³

Lung cancer

Nine out of ten lung cancers are directly related to smoking and the inhalation of second hand smoke is estimated to be responsible for one in four of the lung cancers found in non-smokers.¹⁴

Upper aerodigestive cancer

Smoking is associated with around nine in ten cancers of the lip, oral cavity, pharynx, larynx and oesophagus.¹⁵ All types of tobacco exposure carry a risk of developing these cancers including chewing tobacco, using snuff, smoking cigars or smoking marijuana as well as the more obvious risk from cigarette smoking.

By the age of 75 a smoker has a one in 16 chance of developing these cancers compared to a one in 125 chance in a non-smoker.¹⁶

Stomach and Pancreatic cancer

Smoking contributes to over one in four pancreatic cancers¹⁷ and one in five stomach cancers.¹⁸

Urinary tract cancers

Smoking increases the risk of bladder cancer by three to five times¹⁹ and contributes to two out of three cases in men and one in three cases in women.

The risk of kidney cancer is doubled by smoking. It contributes to one in four cases in men, and one in ten cases in women.²⁰

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The unequal impact of cancer

Cancer has a significant and disproportionate impact on Māori and there are considerable disparities in experiences, quality of health care and outcomes:

- Māori and Pacific Peoples experience greater incidence and significantly greater mortality from all cancers compared to others
- Inequalities in cancer death rates contribute to the significant gap in life expectancy between Māori and non-Māori
- There are disparities in access to cancer services

Māori are nearly twice as likely to die from cancer, even though they are only 18% more likely to have cancer. One reason for this is that Māori are more likely to be diagnosed with cancer at a more advanced stage.

Lung cancer is the leading cause of cancer deaths in New Zealand. The incidence of lung cancer in Māori is the highest in the world. Lung cancer mortality rates have increased in Māori but have decreased for other ethnic groups. The average age of death is also lower (63 years compared to 70 years).

New Zealand survival rates from lung cancer are one of the poorest in the developed world. Lung cancer is the


leading cause of cancer deaths with a five year relative survival rate of 10.2%, considerably worse than Australia (12%) and the USA (15.6%). The five year relative survival rate for Māori is 7.7%.

Multiple factors contribute to the higher mortality rate in Māori including:

- Late presentation
- Delays in treatment
- Low surgical rates for early stage disease

Māori are four times less likely than Europeans to receive curative treatment. In many cases, treatment for Māori is aimed at relieving symptoms.

Focused interventions for Māori are needed to address these disparities.

 See BPJ 18 (December 2008), “The unequal impact of cancer” for further information and references.

Early detection and referral of smoking related cancers

Since the majority of people with cancer will initially present to general practice, GPs have the greatest opportunity to make a difference with early detection and the initiation of speedy referral to specialist services. However, the difficulty is to achieve improved cancer detection without increasing unnecessary referrals, which may reduce access to services for people who need them.

“Lower threshold for referral equals more referral equals more delay to get a hospital appointment. I believe the key point is the quality of the referrals. Referring patients early may cause more patients with self limiting conditions to undergo investigations which do more harm than good to them and the health system. The best test we have in general practice is time BUT we must ensure timely follow up to identify those not resolving”. – GP, Nelson

Detecting cancer

For people presenting with typical symptoms and signs of cancer, the diagnosis and decision for referral is straightforward. However the initial symptoms of some cancers can be difficult to distinguish from the symptoms of other more common disorders or may be vague and non-specific.¹

General guidelines

In people presenting with atypical symptoms or signs, the presence of a risk factor may increase the suspicion of cancer. General risk factors that increase the suspicion of cancer include:

- Māori or Pacific ethnicity²
- Current or ex-smoker
- Known exposure to carcinogen e.g. asbestos
- Previous personal or family history of cancer
- Known pre-cancerous condition e.g. Barrett's oesophagus

If a person presents three or more times with the same symptom or group of symptoms, the GP needs to exclude cancer. Referral to a specialist must be considered.³

Combinations of signs and symptoms have a higher predictive value than a single symptom.³

If common symptoms do not resolve as expected, the initial diagnosis should be reviewed and cancer excluded.⁴

Avoiding delay

Early referral may improve prognosis for people with cancer

Any delay in the time taken from when the first symptom is noticed by the patient, to the start of treatment has potentially negative consequences on the prognosis of cancer.

Delays can occur at several stages and include:

- Failure of some patients to seek help quickly
- Difficulties GPs have in identifying patients with cancer⁵
- Administrative delays in secondary care with the referral process,⁶ accessing investigations and planning

Patient delays

Māori and Pacific peoples,⁷ older people and those from areas of low deprivation⁸ are more likely to be diagnosed with cancer at a more advanced stage⁹ and may by-pass general practice completely and present for the first time at the Emergency Department.¹⁰ It is appropriate to have a higher degree of clinical suspicion in these groups and to examine possible barriers to accessing healthcare.

GP delays

Common reasons for GP delay in referring are insufficient examination, initial misdiagnosis of cancer as a benign self-limiting condition^{11,12} and failure to organise definite follow up.⁵

Delays in investigation and referral

People with features typical of cancer need to be referred without delay. GPs should ensure referrals:

- Are made in a timely manner
- Provide relevant and sufficiently detailed information including patient contact details

- Are followed up promptly to ensure there has been no administrative errors in secondary care that may result in delay

Only consider investigations if this will not delay the referral process. In people with less typical symptoms and signs that might be due to cancer, order investigations urgently.

Making decisions about treatment

Once a possible diagnosis of cancer is made further investigations are required to confirm the diagnosis, stage the cancer and measure the performance status (general health) of the patient before treatment is commenced. Many of these investigations are not available in primary care, except privately, and are usually managed after referral to specialist services.

The cancer diagnosis is usually confirmed with histology or cytology. This is to ensure that the patient does have a malignancy. The precise histopathology will guide prognosis and influence the choice of treatment. For example treatments for small-cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are very different and therefore accurate histological diagnosis is essential.

Treatment decisions are also based on the stage of the cancer. Staging is based initially on clinical examination but is usually clarified with imaging such as CT, MRI or PET scans. The general health of the patient and presence of co-morbidities are also important as they may reflect the prognosis and influence the choice of treatment offered.

Once the information on diagnosis, stage and performance status is available a joint decision can be made between the patient, their family/whanau and the specialist. on whether treatment to cure the patient will be attempted or to offer palliative treatment alone.¹³

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Spotlight on lung cancer

Lung cancer is the fifth most common cancer in New Zealand after breast, prostate, malignant melanoma and colon. However it is the leading cause of cancer mortality in New Zealand men (21%) and the second highest cause in women (16.5%).¹

Lung cancer is rare before the age of 40, more common in Māori (see page 39) and 90% of people with lung cancer are smokers or ex-smokers.^{1,2}

New Zealand has the worst survival rates for lung cancer in the developed world.³

Earlier diagnosis and referral can improve survival rates

The biggest influence on survival is the extent of disease at diagnosis. Lung cancer has one of the lowest survival outcomes of any cancer because over two-thirds of people are diagnosed at a late stage when curative treatment is not possible.

Identifying risk factors for lung cancer

Smoking is the largest preventable risk factor for lung cancer. The risk is increased further with smoking related COPD.⁴

Family history of lung cancer in a first-degree relative is associated with a two-fold increased risk, independent of smoking.⁵

Previous smoking related cancer, especially of the head and neck increases the risk developing lung cancer.⁶

Previous cancer treatment for Hodgkins and non-Hodgkins lymphoma and testicular cancer has been shown to increase the risk of lung cancer. The risk is higher in patients who have been treated with radiotherapy, particularly if they are smokers.⁷

Occupational exposure to carcinogens increases the risk of lung cancer (see sidebar over page).

Identifying symptoms of lung cancer

Making a diagnosis of lung cancer on clinical grounds alone is often not possible. Patients present with a variety of symptoms, mainly respiratory, that are difficult to distinguish from those of other diseases.¹⁰

Red flag symptom – unexplained haemoptysis

Referral for a chest x-ray should be considered in a person presenting with haemoptysis, unless it is the first presentation in an otherwise asymptomatic young person. The most common symptoms of lung cancer are cough, dyspnoea, weight loss and thoracic pain. Haemoptysis and bone pain are also relatively common (Table 1, over page).⁶ Screening individuals without suspicious symptoms is not recommended.¹¹

Occupational exposure to carcinogens

Occupational exposure to carcinogens contributes to 8.5% of lung cancer deaths in New Zealand.⁸ Occupational causes should be considered in people who have a relevant work history (Table 1). N.B. In some cases, treatment may be covered under ACC.

Occupational exposures to lung cancer⁹

Lung carcinogen	Potential exposures
Arsenic	Timber preservation, sheep and cattle dips, horticultural pesticides, glass manufacture and some metal alloys
Asbestos	Plumbers, fitters and ladders, carpenters, builders, clutch and brake repairers, electricians, watersiders, asbestos cement producers, asbestos insulation sprayers and asbestos removal contractors
Chromium VI	Timber preservation, chromium plating and welding stainless steel
Coal tars/pitches	Coal gasification and coke production, foundries, road paving
Environmental tobacco smoke	Bars, restaurants N.B. smokefree legislation has reduced the level of this exposure
Silica	Sand blasting, mines, quarries, foundries, stone work
Soots	Chimney sweeps, building demolition workers, firefighters, any work involving burning of organic materials
Strong inorganic-acid mists containing sulphuric acid	Phosphate acid fertilizer manufacturing

Table 1: Initial signs and symptoms of lung cancer (adapted from NICE⁶)

Common signs and symptoms	Other signs and symptoms
Cough Dyspnoea Weight loss Chest and/or shoulder pain Haemoptysis	Bone pain Finger clubbing Fever Fatigue and weakness Dysphagia Wheezing and stridor Hoarseness Pneumonia Enlarged lymph nodes Superior vena cava obstruction (SVCO)

When to refer


Referral for chest x-ray

A person should be referred urgently for a chest x-ray if they have unexplained haemoptysis or any of the following unexplained persistent signs and symptoms:¹¹

- Chest and/or shoulder pain
- Shortness of breath
- Weight loss or loss of appetite
- Abnormal chest signs
- Hoarseness
- Finger clubbing
- Cervical and/or supraclavicular lymphadenopathy
- Cough
- Features suggestive of metastasis from a lung cancer

The NZGG define “urgent” referral for chest x-ray as being completed and reported within one week.¹²

The NZGG define “persistent” signs and symptoms as those lasting more than three weeks or less than three weeks in people with known risk factors.¹¹

 **Best practice tip:** A person with risk factors for lung cancer who has an x-ray showing consolidation should have a repeat chest x-ray within six weeks to ensure that this has resolved.

Sputum cytology is not recommended for the investigation of lung cancer, except if the patient is too unwell to undergo bronchoscopy. False positives are extremely rare so if positive the likelihood that there is cancer is very high. However it has a very low sensitivity and a negative result cannot be taken to exclude cancer.¹⁰

Referral to specialist care

A person should be referred urgently to a specialist if they have:¹¹

- Persistent haemoptysis and are smokers or ex-smokers aged 40 years or older
- A chest x-ray suggestive of lung cancer
- A normal chest x-ray but where there is a high suspicion of lung cancer (see sidebar)

False negative chest x-rays in people with lung cancer¹²

Overall, chest x-rays may be reported as normal in one in four patients who are found to have lung cancer. The x-ray may be reported as normal but falsely negative for cancer:

- If the lesion is too small to be identified
- If the lesion is hidden behind intra-thoracic structures or the skeleton
- If the x-ray is of poor technical quality or is misreported

If clinical suspicion remains, usually as the result of continuing symptoms or the development of new ones, then further action is warranted. In this situation urgent referral to a specialist for CT scanning and bronchoscopy is recommended.

The case of the tight shirt collar

Recognising superior vena cava obstruction (SVCO)

A 62 year old man presents with a two week history of progressive dyspnoea on exertion, increased snoring and fatigue. He has noticed that his shirt collars have become tight. He is a current cigarette smoker of 15–20 cigarettes a day.

Examination reveals the classic signs of SVCO:

- Oedema of the face and arms
- Flushed face
- Cyanosis
- Dilated and congested veins over the arms, neck and anterior chest wall
- Stridor due to laryngeal oedema
- Papilloedema
- Dilated veins over the abdomen (collateral circulation has developed)
- Headache and confusion due to cerebral oedema

SVCO is a medical emergency and you make an immediate referral to specialist care.

Investigations in primary care are not recommended.

SVCO

SVCO can be due to external pressure or involvement of the vessel by cancer tissue or thrombus. It has mainly malignant causes - the most common is lung cancer.

The superior vena cava carries blood from the head, neck, arms, and upper chest to the heart. When obstructed, the increased venous pressure results in facial, neck and /or upper limb swelling.¹³ Oedema may affect the larynx or pharynx and cause cough, hoarseness and stridor. Symptoms of cerebral oedema include headache, confusion and coma. Over time a collateral circulation develops diverting the venous flow through superficial veins.

Other associated symptoms are chest pain, dizziness, disturbed vision, nausea and nasal stuffiness. Symptoms and signs tend to be aggravated by postures that increase the venous pressure in the upper body such as lying down, bending over or raising the arms above the head. There may also be symptoms from the underlying aetiology e.g. lung cancer.

Symptoms and signs depend on the speed of onset of the compression and the degree of narrowing. Often the symptoms of SVCO develop over many weeks, but in approximately one third of patients the symptoms may develop in two weeks or less. In some cases symptoms improve as collateral circulation develops.

The case of the bloody tissue

A 43 year old woman presents with a one week history of cough and increased sputum production. This is the third time she had visited with a “bad cold”. On this occasion she has noticed some blood in her sputum, which has also become green. She is a current smoker of 20 cigarettes per day. She has been struggling to keep her weight up over the previous few months and relates this to stress at work and the series of “bad colds”.

Examination reveals:

- Erythematous throat with no tonsillar exudate
- Mild soft submandibular lymphadenopathy
- A few scattered rhonchi
- Weight loss of 4 kg since last month

There is no tachycardia, fever, cyanosis or finger clubbing. The trachea is central. There are no focal signs in the chest. Cardiovascular examination is normal.

You should refer for urgent chest x-ray or respiratory assessment.

Haemoptysis

Haemoptysis is the spitting or coughing up of blood that originated in the lungs or bronchi. Patients may be unsure where the blood is coming from and the first step is to differentiate between haemoptysis, pseudo-haemoptysis (spitting of blood not derived from lungs or bronchi, commonly the nasopharynx) and haematemesis.

Haemoptysis is a common symptom. It occurs in up to 40% of people with bronchitis and is also seen in other less serious respiratory conditions. However it is a “red flag” symptom for lung cancer, pulmonary tuberculosis, pulmonary embolism and other serious cardiovascular conditions, as well as systemic diseases and coagulopathies. The likelihood of lung cancer being the cause of haemoptysis is increased when it is recurrent or persistent, and when accompanied by other symptoms such as dyspnoea, weight loss and anorexia and signs such as finger clubbing.¹⁴

The case of the wife who can't sleep

A 77 year old man attends surgery for his routine three monthly repeats. He has started coughing at night and his wife has asked him to get some cough mixture as he is disturbing her sleep. He is only producing a small amount of sputum that is white in colour. He has no weight loss, fever or night sweats. He would also like a repeat GTN spray as he has been using this more often for anterior chest pain but thinks it may be “a dud” as it doesn't seem to be working as well as usual. He has smoked for 50+ years, and has hypertension, ischaemic heart disease and chronic kidney disease. His current medications include: low dose aspirin, cilazapril/hydrochlorothiazide MANE, GTN spray PRN, paracetamol, combivent inhaler 2 puffs QID, beclomethasone inhaler 2 puffs bd.

Examination is unremarkable. Peakflow is 340 L/min, a good result for him. However the history includes two

suspicious features for lung cancer – a new cough and unexplained chest pain which does not appear to be cardiac.

You adopt a stepwise approach to diagnosing the cause of cough.¹⁵

1. You stop ACE inhibitor, check inhaler technique and arrange to review one week later
2. Cough is still present, the patient is already on bronchodilators so you trial promethazine and omeprazole to exclude upper airway cough syndrome (UACS) and GORD¹⁶ and review one week later
3. The cough persists so you refer for chest x-ray

Cough is a common symptom of lung cancer but chronic cough is rarely due to malignancy

It is estimated that less than 1% of patients who visit their doctor with persistent cough will have lung cancer.¹⁷

The majority of lung cancers present to primary care with common respiratory symptoms.¹⁸ The problem for the GP is to filter out very small number of serious cases that warrant urgent specialist referral for investigation of a possible cancer. This is difficult because many symptoms that could indicate cancer, such as cough, also have benign causes and the benign causes are more common.

Acute cough is invariably due to infection or asthma.¹⁹ A cough that has continued for more than three weeks (chronic) is a diagnostic challenge but is still more likely to have a benign cause (Table 2). Apart from current smoking and ACE inhibitors, the three most common causes of chronic cough are upper airway cough syndrome (UACS, previously known as postnasal drip syndrome), asthma and gastro-oesophageal reflux disease (GORD).^{20, 21} The timing of the cough and its character are not predictive of the cause.

Table 2: Causes of chronic cough in adults (adapted from Holmes et al, 2004)²¹

Common causes	Less common causes	Uncommon causes
ACE-I	Bronchiectasis	Aspiration
Upper airway cough syndrome	Eosinophilic bronchitis	Lung cancer and other malignancies
GORD	Post infectious cough	Irritable larynx
Asthma		Persistent pneumonia and abscess
Bronchitis		Tuberculosis
Smoking and other irritants		Sarcoidosis
		Psychogenic cough

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