Risk factors for lung cancer

An overview of the evidence

2014
Risk factors for lung cancer: an overview of the evidence

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Foreword

Lung cancer is the fourth most common cancer diagnosed in both men and women in Australia and the leading cause of cancer death.

*Risk factors for lung cancer: an overview of the evidence* is a comprehensive, evidence-based summary of factors that affect a person’s risk of developing lung cancer, based on a systematic review of the international literature commissioned by Cancer Australia.

This overview aims to increase awareness and understanding of the key lifestyle, environmental and occupational factors that affect lung cancer risk, in addition to the role of family history. The overview also highlights factors where the evidence is either limited or inconsistent in relation to risk of lung cancer.

We anticipate the overview will be a valuable resource to support health professionals, policy makers and the community with evidence about exposure to risk factors for lung cancer, to increase understanding of those who may be at greatest risk of lung cancer, and to inform interventions to ultimately reduce the burden of lung cancer.

Helen Zorbas AO
CEO
Cancer Australia
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Executive summary

In Australia, lung cancer is the fourth most common cancer in both men and women, and the fifth most commonly diagnosed cancer overall.1 Lung cancer causes more deaths than any other cancer, accounting for 18.9% of all cancer deaths.2 A person’s chance of developing lung cancer may be increased by a number of factors, known as risk factors. Risk factors can include behaviours (such as tobacco smoking), chemical agents in the environment or the workplace (such as asbestos, arsenic or radon) or a family history of cancer. Some risk factors are modifiable, meaning the risk can be altered by changing behaviour or adopting safety measures. Other risk factors, such as age, are regarded as non-modifiable.

This overview summarises the evidence for a range of factors that are associated with a person’s risk of developing lung cancer, and is based on a systematic review of published scientific studies.3 The systematic review examined the published research on primary lung cancer up to April 2011 to identify any associations between particular risk factors and lung cancer, and to determine the magnitude of each risk. Pleural mesothelioma, however, is not regarded as a malignant tumour of the lung in the current version of the international coding standards for cancer, and is not considered in this report.

A person’s risk of developing lung cancer can be presented as either absolute risk or relative risk. Absolute risk is a person’s chance of developing lung cancer over a specified time period, while relative risk describes how many times more likely a person exposed to the risk factor is of developing lung cancer than a person who is not exposed to the risk factor. Relative risk also allows comparison of the effects of different risk factors on a person’s likelihood of developing the disease.

Relative risk can be expressed in several different ways. All of the following expressions have the same meaning:
- The relative risk is 1.5.
- The risk is 1.5 times higher.
- There is a 50% greater risk.

Similarly, if the relative risk is 9.0, this means that the risk is 9 times higher in people exposed to the risk factor.

In the case of most risk factors for human diseases, an increase in risk depends on intensity, frequency and duration of exposure, as well as other contextual factors. The interaction of these risk and contextual factors can affect the risk estimate; therefore, relative risk should be considered as indicative of a comparative risk that may vary to some extent from place to place.

Tobacco smoking

Active smoking

Active smoking refers to smoking tobacco in any form, but does not include exposure to other people’s tobacco smoke (passive smoking). There is clear evidence that active smoking significantly increases a person’s risk of developing lung cancer.4 Overall, current smokers are approximately 9 times more likely to develop lung cancer than people who have never smoked (relative risk 9.0).5 Former smokers are almost 4 times more likely to develop lung cancer than people who have never smoked (relative risk 3.9).6 The length of time since quitting smoking varied among studies of ‘former smokers’, but was at least one year in the studies that specified a timeframe.4 The more a person smokes, the greater their risk of developing lung cancer. For example, men who smoke more than 20 cigarettes per day are almost 14 times more likely to develop lung cancer than people who do not smoke (relative risk 13.7)5 while those who smoke fewer than 10 cigarettes per day are 1.4 times more likely to develop lung cancer than non-smokers.5 Smoking can also interact with other lung cancer risk factors to further compound a person’s risk.

Passive smoking

Passive smoking occurs when tobacco smoke is inhaled by people other than through active smoking (i.e. exposure to other people’s tobacco smoke). It is most common in indoor settings, where smoke may not be as easily dispersed as it is outdoors. Passive smoking does not present as pronounced a risk as active smoking, although the risk can still be considerable. Evidence suggests that people who are exposed to passive smoking in their workplace are up to twice as likely to develop lung cancer as people who are not exposed (relative risk 1.2–2.0).6 Exposure to passive smoking at home is also associated with an increase in risk of lung cancer. Women who have never smoked, but have partners who smoke, are 1.3 times more likely to develop lung cancer than women who live with a non-smoking partner.7 The effect on men from the smoking habits of their partners is similar, although not statistically significant—most likely due to the small number of studies that are available.6 There is also emerging evidence to suggest that people exposed to passive smoking as children may be at increased risk of developing lung cancer as adults.4
Environmental and occupational risk factors

Radon
Radon is a naturally occurring radioactive gas. Occupational exposure to radon is most common in uranium miners, who are found to be 1.6–3.8 times more likely to develop lung cancer than people who are not exposed to high levels of radon. The risk increases with increasing exposure, and also with smoking. There is evidence that exposure to moderate amounts of radon in the home can also increase the risk of lung cancer, although not to the same extent as occupational exposure (relative risk 1.3).

Arsenic
Occupational exposure to arsenic most commonly occurs in the mining and manufacturing industries through inhalation of particles that contain arsenic. Evidence suggests that occupational exposure to arsenic compounds in smelter workers, miners (particularly tin and gold miners) and production workers increases the risk of lung cancer. Generally, a person’s risk increases with increasing levels and duration of exposure. Smoking appears to further increase the risk of lung cancer in people who are exposed to arsenic in their workplace. There is also evidence that high levels of arsenic in drinking water in some populations are associated with an increased risk of lung cancer; however, these findings are not generalisable to developed countries such as Australia, where concentrations of arsenic in drinking water fall well within the World Health Organization’s prescribed safe levels. Studies suggest that smoking further increases the risk of lung cancer after exposure to arsenic in drinking water, particularly at high concentrations of arsenic.

Polycyclic aromatic hydrocarbons
Polycyclic aromatic hydrocarbons (PAHs) are byproducts of burning organic material, such as coal, crude oil, natural gas, garbage and tobacco. Sources of PAHs include urban and industrial air pollution, tobacco smoke and diet. People working in particular occupations and industries may be exposed to high levels of PAHs. Industries associated with a higher risk of lung cancer from PAH exposure include coal gasification, coke production and carbon black production (relative risk for workers in these industries is approximately 1.2–2.0). It is not clear whether the length of time that a person is exposed to PAHs affects their risk.

Cadmium
Cadmium is a metal that occurs naturally in the Earth’s crust and in sea water, and is used in a range of industrial applications. Evidence suggests there is a modest increase in risk of lung cancer associated with cadmium exposure; however, the high level of variability in studies makes it difficult to measure the overall risk. It is also difficult to define the risk of occupational cadmium exposure, although it appears that exposure to cadmium fumes or mist is associated with a greater risk than exposure to cadmium dust (relative risk 2.1 compared with 0.7–1.0 for cadmium dust). Cadmium can also accumulate in soil, particularly in areas near industrial sources of cadmium. One study suggests that people who are highly exposed to cadmium in their homes (as a result of proximity to zinc smelters) have a higher risk of developing lung cancer than people who live in unexposed areas.

Asbestos
Asbestos is a naturally occurring mineral that was once commonly used in building materials. The risk of lung cancer is increased by inhaling asbestos fibres, particularly in high doses or over long periods of time. Overall, people who are exposed to asbestos as part of their occupation are 1.3–2.0 times more likely to develop lung cancer than unexposed workers (relative risk 1.3–2.0). There is strong evidence that smoking (or a history of smoking) compounds the risk of lung cancer in people already at increased risk due to their high exposure to asbestos. People who have asbestosis (a disease in which the lungs become inflamed and scarred as a result of exposure to asbestos) have a higher risk of lung cancer than the general population; their lung cancer risk is also higher than that of people exposed to asbestos who do not have asbestosis. Results from studies on non-occupational exposure to asbestos are variable: some studies show an increased risk and others do not. It is also not clear whether the type of asbestos fibre affects the risk of lung cancer.

Silica
Silica is a term describing a group of minerals that contain silicon and oxygen. The small dust particles formed by some types of these minerals can be inhaled and are associated with lung cancer. Exposure to silica can occur in a person’s occupation, particularly in industries such as foundling, pottery, sandblasting, construction, quarrying, and clay and glass manufacturing and processing. People who are exposed to silica are approximately 1.2–1.3 times more likely to develop lung cancer than people who are not exposed to silica. Studies suggest that higher
Silica contd.

Intensity and duration of silica exposure increase the risk of lung cancer. People with silicosis (a disease that causes scarring of the lungs, caused by repeated and prolonged exposure to silica) are approximately twice as likely to develop lung cancer as people who are exposed to silica but do not have silicosis. Smoking also increases the risk of lung cancer from exposure to silica, and this risk increases the more a person smokes.

Iron and steel founding

Workers in iron and steel founding (the process of pouring molten metal into a mould to create a new shape or object) may be exposed to several risk factors for lung cancer. Overall, evidence suggests that iron and steel foundry workers are 1.3–1.4 times more likely to develop lung cancer than people who do not work at foundries. Exploring particular occupations, one study found that blast furnace workers had a higher risk of lung cancer, but no significant risk elevation was linked with workers in the manufacture of coke batteries, steel mills, lamination, steel foundries, maintenance furnaces or facilities producing coke byproducts. Studies have found that people who worked in the foundry industry for less than 10 years generally did not have a higher risk of developing lung cancer, but people who have worked in iron and steel founding for more than 30 years are almost twice as likely to develop lung cancer as people who do not work in the industry (relative risk 1.9). Foundry workers who smoke have a higher risk of developing lung cancer than foundry workers who do not smoke, and the risk increases with increased smoking.

Nickel

People who work with nickel in their occupations can be exposed to high levels of nickel through fumes, dust and mist. Evidence suggests that occupational exposure to nickel represents a modest increase in the risk of lung cancer. However, the variability in studies included in the review makes it difficult to provide a clear, quantifiable risk. The risk of developing lung cancer due to nickel exposure appears to increase with increasing levels and duration of exposure. One study found that exposure to nickel for more than 20 years was associated with a relative risk of lung cancer of 1.6 compared with no exposure to nickel. Smokers who are exposed to nickel also appear to have a higher risk of developing lung cancer than non-smokers who are exposed to nickel, and this risk increases with increasing nickel exposure.

Beryllium

Beryllium is a naturally occurring metal that is found in rocks, coal, oil, volcanic dust and soil. Exposure to beryllium can be an occupational risk in some specialised occupations, such as mining and processing beryllium ores, manufacturing and processing beryllium alloys or compounds, or working with metals that contain beryllium. Evidence suggests that occupational exposure to beryllium represents a modest risk factor for lung cancer, and any increase in risk is dependent on a relatively high level of exposure. However, all studies of beryllium exposure included in the systematic review were of men who worked in beryllium processing plants in the United States between 1940 and 1970. Overall, the relative risk of developing lung cancer in these men was 1.0–1.5. In Australia today, it is unlikely that workers or people in their domestic environments would be exposed to beryllium at levels that may increase the risk of lung cancer.

Painting as an occupation

Inhalation of paint particles or fumes is associated with an increased risk of lung cancer, and people who work with paint every day in their occupation have higher exposure than people who do not work as painters. People who work in the painting trade may also be exposed to other substances, such as asbestos, chromium and cadmium, that may increase their risk of developing lung cancer. The combined results of several studies show that, overall, people who work as painters are 1.3 times more likely to develop lung cancer than people who do not work as painters. There was inconsistent evidence regarding the impact of duration of employment as a painter or a spray painter on lung cancer risk.

Chromium VI

Exposure to chromium VI (a toxic form of chromium) can occur in occupations that involve the production, use and welding of chromium-containing alloys (such as stainless steel and high-chromium steel); the production and use of chromium-containing paints (such as in the aerospace, construction and maritime industries); electroplating; catalysts; chromic acid and pesticides. Combined results of many studies indicate that people who are exposed to chromium VI are at approximately 1.2 times greater risk of lung cancer than people who are not exposed (standardised mortality rate 1.2). There is insufficient evidence to determine whether duration of exposure to chromium VI affects the risk of developing lung cancer, but evidence does suggest that the amount of chromium exposure may have a greater effect on risk than duration of exposure.
Air pollution

Air pollution in outdoor air includes fine particulate matter and gases, mainly from urban pollution and vehicle exhaust. There is evidence that exposure to fine particulate matter in the air increases a person’s risk of lung cancer by 1.2 times after one year of exposure. This risk does not appear to increase over time—the relative risk after 21 years’ exposure to fine particulate matter is not significantly different from the risk after one year’s exposure. Sulfur dioxide and nitrogen dioxide (other gaseous components of air pollution) do not appear to be associated with an increased risk of lung cancer. However, there is mixed evidence as to whether other nitrogen oxides are associated with a small increase in risk. There has been no evidence of an increase in lung cancer risk in studies of people living near busy or major roads.

Diesel exhaust as a risk factor for lung cancer

In June 2012, the International Agency for Research on Cancer (IARC) identified that there is sufficient evidence that exposure to diesel engine exhaust is associated with an increased risk of lung cancer. While large populations are exposed to diesel exhaust in everyday life, whether as part of their occupation or through exposure to motor vehicle and other diesel engine exhausts in the ambient air, the main studies that led to IARC’s conclusion were in highly exposed workers. Exposure to diesel exhaust is not included as a risk factor in this overview, as the systematic review was conducted before IARC’s classification of diesel engine exhaust as a substance with sufficient evidence to be causally associated with lung cancer.

Family history

Families share environmental and behavioural characteristics as well as genetic traits, and a person’s knowledge of a history of lung cancer within their family can help to increase understanding of these shared risks. Genomic research and the application of genetic technologies are emerging areas of research that are increasing our understanding of cancer biology and of the genetic factors associated with lung cancer. There is also potential for the application of genomic approaches to management of cancer risk. This systematic review, however, was limited to studies of family relationships. There is evidence to suggest that a person who has a family member with lung cancer is approximately twice as likely to develop lung cancer as someone without a family history of the disease. The results suggest that the risk appears to be more significant if two or more family members have had lung cancer or if a person’s mother had lung cancer.
Factors with limited evidence of an association with lung cancer

Factors that have not been found to be associated with an increased risk of lung cancer, including where the studies are either of poor quality or have conflicting results:

- consumption of red meat and processed meat
- alcohol consumption
- dietary and blood cholesterol
- exposure to birds
- exposure to wood dust
- physical activity.

What does this mean for individuals?

The evidence discussed in this overview outlines the risk factors for lung cancer at a population level—that is, the evidence is based on averages from large groups of people. The relative risks describe the probability of developing lung cancer in a certain group of people over a certain period of time, but they cannot tell us which individual person might develop lung cancer.

This means that a person can be exposed to a risk factor, or several risk factors, and not develop lung cancer during their lifetime. On the other hand, a person may never have been exposed to any known risk factors, but they might develop lung cancer. In addition, even if a person with lung cancer has a risk factor, it is usually hard to know how much that risk factor contributed to the development of the cancer.

This overview provides consumers, health professionals and policy makers with evidence-based information about risk factors for lung cancer. By understanding and recognising the risk factors, people can make informed decisions about exposure to these factors.

Levels of evidence

For each risk factor, the inclusion and presentation of the findings has been broadly ordered according to the National Health and Medical Research Council (NHMRC) levels of evidence:

- Level I—a systematic review of Level II studies
- Level II—a prospective cohort study
- Level III-1—an ‘all or none’ study
- Level III-2—a retrospective cohort study
- Level III-3—a case–control study
- Level IV—a cross-sectional study or case series.

These levels of evidence for the risk factors are shown in the summary of relative risks table (page x - xi) and in the risk graphics shown for each of the risk factors in this overview.
# Summary of relative risks

## Active smoking

<table>
<thead>
<tr>
<th>Smoking:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;20 cigarettes per day (Level I)</td>
<td>13.7–24.1</td>
</tr>
<tr>
<td>Current smokers overall (Level I)</td>
<td>9.0</td>
</tr>
<tr>
<td>Former smokers overall (Level I)</td>
<td>3.9</td>
</tr>
<tr>
<td>10–19 cigarettes per day (Level I)</td>
<td>2.7–1.3</td>
</tr>
<tr>
<td>&lt;10 cigarettes per day (Level I)</td>
<td>1.4–1.5</td>
</tr>
</tbody>
</table>

## Radon

<table>
<thead>
<tr>
<th>Exposure:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uranium miners, 40–240 WLM (Level II)</td>
<td>1.6–3.8</td>
</tr>
<tr>
<td>Residential exposure ≥ 250 Bq/m³ (Level II)</td>
<td>1.4</td>
</tr>
</tbody>
</table>

## Arsenic

<table>
<thead>
<tr>
<th>Exposure:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational with longer duration of employment (Level II, III)</td>
<td>2.0–3.0</td>
</tr>
<tr>
<td>Occupational exposure overall (Level II, III)</td>
<td>1.5–1.7</td>
</tr>
</tbody>
</table>

## Polycyclic aromatic hydrocarbons

<table>
<thead>
<tr>
<th>Exposure:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coke production and coal gasification workers (Level II)</td>
<td>1.2–2.3</td>
</tr>
</tbody>
</table>

## Cadmium

<table>
<thead>
<tr>
<th>Exposure:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>High exposure to cadmium fumes or mist (Level III)</td>
<td>2.1</td>
</tr>
</tbody>
</table>

## Asbestos

<table>
<thead>
<tr>
<th>Exposure:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occupational exposure to asbestos (Level II)</td>
<td>1.3–2.0</td>
</tr>
</tbody>
</table>

## Silica

<table>
<thead>
<tr>
<th>Exposure:</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>People with silicosis (Level I)</td>
<td>2.0</td>
</tr>
<tr>
<td>Exposure to silica for more than 26 years (Level II)</td>
<td>1.7</td>
</tr>
<tr>
<td>Occupational exposure in various industries (Level I)</td>
<td>1.2–1.3</td>
</tr>
</tbody>
</table>
Summary of relative risks cont.

### Passive smoking
- High workplace exposure (Level I) 2.0
- Women exposed to their partner’s smoking (Level I) 1.3
- Workplace exposure overall (Level I) 1.2

### Family history
- Any family member with lung cancer (Level I) 2.0

### Iron and steel founding
- Foundry workers employed for more than 30 years (Level I) 1.9
- All relevant industries (Level I) 1.3–1.4

### Nickel
- Duration of exposure more than 20 years, across all relevant industries (Level I) 1.6
- Occupational exposure in relevant industries (Level I) 1.3

### Beryllium
- Occupational exposure in beryllium processing plants (Level I) 1.0–1.5

### Painting as an occupation
- Employment as a painter (Level I) 1.3

### Chromium VI
- Any exposure to chromium VI (Level I) 1.2

### Air pollution
- One year of exposure to 10 μg/m³ of fine particulate matter (PMₐ₅₅) (Level I) 1.2
Background

What is lung cancer?

Lung cancer is a disease where cells in the lungs become abnormal and grow out of control, forming a malignant tumour, or cancer. As the cancer grows, it can impair lung function and spread to other parts of the body through a process known as metastasis. There are different types of lung cancer, beginning in different types of cells in the lungs. Of all lung cancers diagnosed in 2007, non–small cell carcinoma (i.e. squamous cell carcinoma, adenocarcinoma and large cell carcinoma) represented 64% of lung cancers in males and 61% in females, small cell carcinoma represented 11% of lung cancers in males and 13% in females, and other types of lung cancer accounted for the remaining 25% of lung cancer cases.1

In this overview, lung cancer refers to all forms of primary lung cancer but does not include pleural mesothelioma, which is a rare type of cancer affecting the membrane that covers and protects the lungs (the pleura). Pleural mesothelioma is almost always caused by exposure to asbestos.58 Because pleural mesothelioma occurs in the lining of the lung, it is sometimes referred to as lung cancer. However, pleural mesothelioma is not regarded as a malignant tumour of the lung in the current version of the international coding standards for cancer and is not considered in this overview.1 Cancer that originated in other parts of the body can also spread to the lungs, but these secondary cancers are not classified as lung cancer and are not included in this overview.

Lung cancer in Australia

In Australia, lung cancer is the fourth most common cancer diagnosed in both men and women, and the fifth most commonly diagnosed cancer overall.1 In 2009, 8.9% of all new cancers were lung cancers, with 10 193 people diagnosed (6034 men and 4159 women).59 Men are almost twice as likely to be diagnosed with lung cancer as women,60 however, since 1982, the rate of lung cancer in men has been decreasing, while the rate in women has been increasing.1

Lung cancer causes more deaths in Australia than any other cancer.7 A total of 8099 Australians died from lung cancer in 2010 (4934 men and 3165 women), comprising nearly 19% of all cancer deaths.12 Since 1982, mortality rates for lung cancer have decreased in men, but increased in women.59 Worldwide, lung cancer is the leading cause of cancer death, accounting for more than 1.37 million deaths per year.61

Symptoms of lung cancer can often be vague and non-specific, which can hinder early diagnosis and treatment.62 Although survival rates have gradually increased since 1982, they remain poor, with about 14% of people diagnosed likely to be alive five years after their diagnosis.63 Poor survival is due at least in part to the relatively high proportion of people diagnosed at an advanced stage, when the cancer has already spread to other parts of the body and is difficult to treat successfully. Poor survival outcomes for people with lung cancer are reflected internationally.61

The risk of developing lung cancer increases with age. In 2009, 85% of new lung cancers in men and 81% in women were diagnosed in people aged 60 years or older.64 In 2009, the average age of first diagnosis was 71 years for men and 70 years for women.59 Overall, about 1 in 13 men and 1 in 22 women in Australia will be diagnosed with lung cancer by the age of 85.59 However, people’s behaviours, occupations or family histories can affect their risk of developing lung cancer.

What is a risk factor?

A risk factor is any factor that is associated with an increase in someone’s chances of developing a certain condition, such as cancer. Some risk factors are modifiable, such as lifestyle or environmental risk factors, and others cannot be modified, such as family history and inherited factors.

How do we measure risk?

Risk factors may also be called hazards. The extent of harm from the risk factor and the consequences of this harm are expressed in terms of how hazardous the risk factor is (i.e. its potential to cause harm). However hazardous a risk factor is, it will only pose a threat when other factors combine to allow a person to be exposed to it. ‘Risk’ measures the likelihood of harm associated with exposure to the hazard.

In the case of most risk factors for human diseases, an increase in risk depends on both the intensity of exposure (how much of the risk factor a person is exposed to at one time) and the frequency or duration of exposure (how often and for how long a person is exposed to the risk factor over their lifetime).

Absolute risk

Absolute risk is a person’s chance of developing a specific disease over a particular period of time. A person’s absolute risk of disease is estimated by examining a large number of people similar in some respect (such as age or gender) and counting the number of individuals in this group who develop the disease within a defined period.
Absolute risk contd.
For example, the risk of developing lung cancer by the age of 85 years for an Australian man is 1 in 13 and for an Australian woman is 1 in 22. This means that for every 13 men who live to 85, one of them will have been diagnosed with lung cancer during his lifetime, and, similarly, for every 22 women who live to 85, one of them will have been diagnosed with lung cancer during her lifetime.59

Absolute risk is a measure of the size of the risk outcome overall. This can be useful to understand the importance of a risk factor and to make decisions about exposure to it.

Relative risk
Relative risk compares the absolute risk of a group of people who are exposed to a risk factor with the absolute risk of a group of people who are not exposed to the risk factor. For example, you could compare the risk of lung cancer in people who smoke with the risk of lung cancer in people who do not smoke.

This is an important distinction, because a certain proportion of people in the unexposed group will also develop the disease, even though they have never been exposed to that risk factor. Relative risk indicates how many times more likely a person in the exposed group is to develop the disease. Importantly, for a disease such as lung cancer, relative risk also allows comparison of the effects of different risk factors on a person’s likelihood of developing the disease.

In mathematical terms, relative risk is the absolute risk in the exposed group divided by the absolute risk in the unexposed group. If the relative risk is 1, this indicates that the exposed group has the same chance of developing the disease as the unexposed group. If the relative risk is greater than 1, the exposed group is at greater risk, and if the relative risk is less than 1, the exposed group has a lower risk than the unexposed group.

Relative risk can be expressed in several different ways. The following expressions all have the same meaning:

- The relative risk is 1.5.
- The risk is 1.5 times higher.
- There is a 50% greater risk.

Similarly, if the relative risk is 9.0, this means that the risk is 9 times higher.

<table>
<thead>
<tr>
<th>Exposed group</th>
<th>Relative risk</th>
<th>Unexposed group</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 people out of 10 are affected in each group</td>
<td>2 (number of affected people) (\div) 10 (number of people in the group) = 0.2</td>
<td>Absolute risk in each group is 0.2</td>
</tr>
<tr>
<td>Relative risk is 0.2 (\div) 0.2 = 1</td>
<td>The risks are the same in both groups</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposed group</th>
<th>Relative risk</th>
<th>Unexposed group</th>
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<tbody>
<tr>
<td>5 people are affected in the exposed group, compared with 2 people in the unexposed group</td>
<td>Relative risk is 0.5 (\div) 0.2 = 2.5</td>
<td>The people in the exposed group are 2.5 times (or 250%) more likely to be affected than the people in the unexposed group</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exposed group</th>
<th>Relative risk</th>
<th>Unexposed group</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 person in the exposed group is affected, compared with 3 people in the unexposed group</td>
<td>Relative risk is 0.1 (\div) 0.3 = 0.3</td>
<td>The people in the exposed group are 0.3 times as likely (or 70% less likely) to be affected than the people in the unexposed group</td>
</tr>
</tbody>
</table>

Figure 1 Calculating relative risk
Relative risk contd.
In the case of most risk factors for human diseases, an increase in risk depends on intensity, frequency and duration of exposure, as well as other contextual factors. The interaction of these parameters can affect the precision of the risk estimate; therefore, the relative risk should be considered as an indication of how to interpret the evidence in the context of these parameters, not as a definitive measurement.

In this overview, relative risk is reported to one decimal place. This is usually accompanied by a 95% confidence interval (95% CI), which is a measure of the precision of the risk estimate (i.e. the extent to which it is likely to vary by chance)—the narrower the interval, the more precise the estimate of the risk, and the less likely that the risk would be subject to chance variation.

About this overview
This overview provides consumers, health professionals and policy makers with evidence-based information about risk factors for lung cancer. Understanding and recognising these risk factors can help people make informed decisions about their exposure to these factors.

Data sources
This overview is a summary of the systematic review conducted for Cancer Australia by the Joanna Briggs Institute at the University of Adelaide. The systematic review is available on the Cancer Australia website at www.canceraustralia.gov.au. The systematic review examined the published research on lung cancer up to April 2011, to identify any associations between particular risk factors and lung cancer, and to determine the magnitude of each risk. In the systematic review, the level of evidence available was assessed for each risk factor, using the National Health and Medical Research Council (NHMRC) levels of evidence for aetiology.67

- Level I - a systematic review of Level II studies
- Level II - a prospective cohort study
- Level III-1 - an 'all or none' study
- Level III-2 - a retrospective cohort study
- Level III-3 - a case-control study
- Level IV - a cross-sectional study or case series

The International Agency for Research on Cancer (IARC) Monographs on the Evaluation of Carcinogenic Risks to Humans published to 2011 were used as a main source of evidence and guided the identification of risk factors to be studied in this overview (see Appendix 1 for more detail of IARC classifications of risk factors). In addition, a multidisciplinary expert advisory group assisted in the prioritisation of risk factors to be studied. In guiding this process, the group considered the likelihood of exposure to respective risk factors in Australia, the likely population exposures to these risk factors, the likely risks associated with these exposures, the quality of available evidence from which to draw robust conclusions, and the potential for modifiability. This overview refers to cancers other than lung cancer where IARC has identified that there is sufficient evidence of a causal relationship between exposure to the agent and those cancers.

Most studies reported risks as relative risks. If risks were expressed as odds ratios, standardised mortality ratios or another estimate of risk or effect, this is specified in the text of this overview, but these measures were interpreted similarly to relative risks (see the systematic review for more details). A glossary of terms, including odds ratios and standardised mortality ratios, is provided at the end of this overview.
Presentation of relative risk estimates

The systematic review examined published research of studies of relative risk and other measures of association on risk factors for lung cancer. These studies were conducted in numerous contexts across various population groups and with a mixture of methodologies to explore the impact of exposure to the risk factor and the potential impact of tobacco smoking status on relative risk for lung cancer for that risk factor. For some risk factors, the systematic review identified a wide range of heterogeneous data (i.e. a high level of variability between studies). In some cases, the authors drew on published meta-analyses to determine overall relative risk estimates, and, in others, the authors conducted their own meta-analysis of studies to synthesise findings.

The risk estimates represented in the risk graphics at the top of each of the risk factors in this overview reflect the synthesised findings as identified in the systematic review. More details pertaining to the range of the relative risks identified are summarised in the body of the overview. The risk graphic also identifies the risk factors where tobacco smoking interacted with that risk factor to increase lung cancer risk.

What does this overview mean for individuals?

The evidence discussed in this overview outlines the risk factors for lung cancer at a population level—that is, the evidence is based on averages from large groups of people. The relative risk describes the probability of developing lung cancer of a group of people that share a particular risk factor, compared with those without this risk factor. Information about risk factors cannot predict whether an individual person will actually develop lung cancer.

This means that a person can be exposed to a risk factor, or several risk factors, and not develop lung cancer during their lifetime. On the other hand, a person may never have been exposed to any known risk factors but still develop lung cancer. In addition, even if a person with lung cancer has a risk factor, it is usually hard to know how much that particular risk factor contributed to the development of the cancer.
Tobacco smoking

Active smoking

Active smoking refers to smoking tobacco through any means, including cigarettes, cigars, pipes, bidis and waterpipes. It does not include exposure to other people’s tobacco smoke (known as passive smoking), which is addressed as a separate risk factor in this overview.

IARC has identified that there is sufficient evidence to indicate that tobacco smoking is a cause of lung cancer. In Australia, about 90% of lung cancer in males and 65% in females is estimated to be a result of active smoking. IARC has also identified that there is sufficient evidence to indicate that tobacco smoking can cause cancer of the oral cavity, nasopharynx, oropharynx and hypopharynx, nasal cavity and accessory sinuses, larynx, oesophagus, stomach, pancreas, colorectum, liver, kidney (body and pelvis), ureter, urinary bladder, uterine cervix and ovary (mucinous), and myeloid leukaemia, and that parental smoking is a cause of hepatoblastoma in children. Also, IARC has identified a positive association between tobacco smoking and breast cancer risk in women.

Exposure to active smoking

In 2011–12, one in six (16.3%) Australians aged 18 years and over smoked tobacco daily (about 2.8 million people). A further 2% reported that they smoked tobacco less than daily, and 31% reported that they were ex-smokers.

In Australia, the smoking rate has declined since the second half of the last century. In 1964, an estimated 58% of males smoked, with this decreasing to 18% in 2011–12. For females, the overall smoking rate increased slightly in the 1960s and 1970s, which was followed by an appreciable decline in the smoking rate from 31% in 1980 to 14% in 2011–12. Decreases in smoking rates have occurred across all age groups, and particularly among people aged less than 45 years.

What is the risk?

Overall risk

There is clear evidence that active smoking significantly increases a person’s risk of developing lung cancer. Current smokers are approximately 9 times more likely to develop lung cancer than people who have never smoked (relative risk 9.0, 95% CI 6.7–12.1). Although the risk of lung cancer is lower for former smokers than active smokers, it remains significant, with former smokers almost 4 times more likely to develop lung cancer than people who have never smoked (relative risk 3.9, 95% CI 2.8–5.3). The length of time since quitting smoking varied among studies of former smokers, but was at least one year in the studies that specified a timeframe.

The more a person smokes, the greater their risk of developing lung cancer. In males, for example, a meta-analysis found that those men who smoke fewer than 10 cigarettes per day are 1.4 times more likely to develop lung cancer than non-smoking men (relative risk 1.4, 95% CI 1.3–1.5). This relative risk increases to 2.7 (95% CI 2.1–3.4) for men who smoke 10–19 cigarettes per day, and 13.7 (95% CI 7.4–25.5) for men who smoke more than 20 cigarettes per day. Similarly, women who smoke fewer than 10 cigarettes per day are 1.5 times more likely to develop lung cancer than...
Overall risk contd.

non-smoking women (relative risk 1.5, 95% CI 1.4–1.6). This relative risk increases to 3.3 (95% CI 2.6–4.2) for women who smoke 10–19 cigarettes per day and 24.1 (95% CI 12.7–45.9) for women who smoke more than 20 cigarettes per day. Despite these apparent differences in risk between the sexes, there is insufficient evidence overall to determine whether women have a higher risk of developing lung cancer from smoking than men.

Overall, the relative risk of lung cancer increases by 0.07, or 7%, for each additional cigarette smoked per day (relative risk 1.07, 95% CI 1.06–1.08).

The length of time that a person has been smoking is likely to affect their risk of developing lung cancer. However, because individual studies categorised the length of time that people smoked in different ways, the results cannot be combined to determine the relative risks for smoking for different lengths of time.

Risk from other forms of tobacco smoking

People who smoke mentholated cigarettes have the same relative risk of developing lung cancer as people who smoke non-mentholated cigarettes.

Studies that investigated the risk of lung cancer from smoking a waterpipe (also known as an arguileh, hookah, narghile or shisha) were generally of poor quality. However, overall they indicate that smoking a waterpipe increases the risk of lung cancer (relative risk 2.1, 95% CI 1.3–3.4).

Interaction with other risk factors for lung cancer

Smoking is not only a risk factor for lung cancer in itself, but can also interact with other risk factors to further compound the risk. For example, studies suggest that smokers and former smokers who are occupationally exposed to radon have a higher risk of developing lung cancer than from exposure to either radon or smoking alone. Evidence also suggests that smoking has an additive effect on the risk of developing lung cancer due to exposure to asbestos, arsenic, occupational radon, polycyclic aromatic hydrocarbons, silica, nickel, a positive family history, and iron and steel founding. See the relevant risk factors in this overview for details.
Passive smoking is also known as involuntary smoking, exposure to environmental tobacco smoke or second-hand smoke, and tobacco smoke pollution. It occurs when tobacco smoke is inhaled by a person other than through active smoking (i.e. exposure to other people's tobacco smoke).

IARC has identified that there is sufficient evidence to indicate that passive smoking is a cause of lung cancer.4

**Exposure to passive smoking**

Passive smoking is most common in indoor settings, where smoke may not be as easily dispersed by the air as it is outdoors. Before smoking bans were introduced in indoor public places, smoking was permitted in restaurants, bars and a variety of other indoor areas. People who visited or worked in these places may have been exposed to passive smoking. Exposure can also occur in the home—for example, if one or more people in a household smoke but others do not.

**What is the risk?**

**Workplace exposure**

Passive smoking does not present as pronounced a risk as active smoking, although the risk can be significant. Evidence suggests that people who are exposed to passive smoking in their workplace are 1.2 times more likely to develop lung cancer than people who are not exposed in their workplace (relative risk 1.2, 95% CI 1.2–1.3).6 This relative risk increases to 2.0 (95% CI 1.3–2.6) for people who are highly exposed to passive smoking in the workplace.6 However, it is difficult to define what exactly constitutes ‘high’ workplace exposure, as the highest exposure categories varied significantly among studies included in the meta-analysis.6

The length of time a person is exposed to passive smoking also affects their risk of developing lung cancer. Analysis of data suggests that people who are exposed to 45 years of passive smoking in the workplace are approximately 1.6 times more likely to develop lung cancer than people who have not been exposed (relative risk 1.6, 95% CI 1.5–1.8).6

**Exposure in the household**

Most studies on passive smoking as a result of exposure to smoke from another person in the household involve women who have never actively smoked but are exposed to passive smoke from their partners. In one analysis, 45 out of 55 studies (82%) showed that non-smoking women who lived with a partner who smoked were more likely to develop lung cancer than women who lived with a non-smoking partner, with an overall relative risk of 1.3 (95% CI 1.2–1.4).7 The effect on men from the smoking habits of their partners was similar, although not statistically significant—most likely due to the small number of studies that contributed data.8

**Exposure from parents during childhood**

The systematic review found that there was little evidence to suggest that exposure to tobacco smoke during childhood increases the risk of lung cancer in adulthood. An analysis of 11 studies found little evidence of increased risk of lung cancer, regardless of which parent smoked.68 However, IARC has identified that there is emerging evidence to suggest that exposure to second-hand smoke among children may increase the risk of lung cancer in adulthood.4
Environmental and occupational risk factors

Radon

Radon is a naturally occurring radioactive gas that forms underground and disperses into the atmosphere. It decays naturally into particles that can attach to dust and other aerosols. If these particles are inhaled, they can deposit in the lungs and expose a person to radiation. This can cause a variety of damage to cells and DNA that can contribute to cancer. IARC has identified that there is sufficient evidence to indicate that radon is a cause of lung cancer.

Exposure to radon

Radon exposure can occur during a person’s occupation, particularly uranium miners. Radon forms from the radioactive decay of uranium, and is therefore common in uranium mines. In 2011, approximately 8000 Australians were employed in the uranium mining and milling industry in occupations with a risk of radiation exposure. The radiation doses of these workers are assessed and recorded regularly by their employers, and entered in the Australian National Radiation Dose Register.

Radon forms part of the natural background radiation on Earth, and all people are exposed to extremely small amounts of it. The radon level in any particular place in the world depends on the nature of the underlying rock and soil; therefore, radon exposure in Australia will be different from that in other countries. Because radon can accumulate in enclosed spaces, including houses, residential exposure to radon can be substantial—although levels in Australia are lower than in many other countries. The average radiation level in homes in Australia is 11 becquerels per cubic metre (Bq/m³), but levels can range from 1 to more than 400 Bq/m³.

What is the risk?

Occupational radon exposure

Many studies of occupational exposure to radon use the ‘working level month’ (WLM) as a way of measuring the length of time a person is exposed to radon, and the dose of radiation they were exposed to. A ‘working level’ is a defined amount of radiation, and a WLM refers to exposure to a working level of radiation for 170 hours (the typical working month).

Evidence suggests that uranium miners are at risk of developing lung cancer from radon exposure. Risk in these miners increases in a dose-dependent manner with increased levels of exposure. Studies in Europe showed that uranium miners with exposure of 40–240 WLM had a relative risk of developing lung cancer of 1.6–3.8. Another study showed that this risk increased to 4.6 (95% CI 2.3–9.4) at exposures of more than 1000 WLM. Other types of miners can also be exposed to radon. Iron ore miners have a higher risk of developing lung cancer due to radon exposure than the general population, although generally not to the same extent as uranium miners. However, studies informing the risk of lung cancer in iron ore miners were conducted in Sweden, the United States, the United Kingdom and China, with no included studies conducted in Australia.
Occupational radon exposure contd.

Effect of smoking

Studies suggest that smokers and former smokers who are occupationally exposed to radon have a higher risk of developing lung cancer than from radon exposure or smoking alone. In particular, evidence shows that uranium miners who smoke increase their lung cancer risk by approximately 7 times.3,12 The relative risk of lung cancer for people who have never smoked increases with increasing radon exposure; however, these risks are consistently higher in former smokers, and even higher in current smokers.12

Residential radon exposure

There is evidence that residential exposure to radon increases a person’s risk of developing lung cancer, although generally not to the same extent as occupational exposure. Most studies of exposure to radon in the home measure the radon concentration in Bq/m$^3$ over 5 to 30 years, rather than the occupational measure of WLM.

Various syntheses of studies from different continents suggest that people exposed to radon concentrations of more than 250 Bq/m$^3$ are 1.4 times more likely to develop lung cancer than unexposed populations (relative risk 1.4, 95% CI 1.2–1.7).13 Studies in Europe have estimated that residential radon exposure increases the risk of lung cancer by 8% for every 100 Bq/m$^3$ of radon exposure over 5 to 30 years.70

Effect of smoking

There is evidence to suggest that the risk of developing lung cancer from residential exposure to radon may also be increased by smoking, although not to the same extent as in miners. One study shows that, for smokers and non-smokers exposed to the same radon concentration (100 Bq/m$^3$) for at least five years in China, the relative risk increases with the number of cigarettes smoked per day. People who smoked 10 cigarettes per day over 30 years had a risk of 2.9 (odds ratio, 95% CI 2.2–4.0), while people who smoked 20 cigarettes per day over 40 years had a relative risk of 4.5 (95% CI 2.8–7.1).74 Another study suggests that people living in homes in Sweden with environmental tobacco smoke and a radon concentration of 140 Bq/m$^3$ have a relative risk of developing lung cancer of 2.1 (95% CI 1.2–3.7).75
Arsenic

Arsenic is a chemical found in the Earth’s crust. It can contaminate air, water and soil as a result of natural causes (such as volcanic activity) or human activities (such as mining, smelting and burning fuel).14 Arsenic can enter the body through contaminated food, water or air.14 It is thought that the arsenic reacts in the body to form free radicals, which can damage cells and DNA, and contribute to cancer.14

IARC has identified that there is sufficient evidence to indicate that arsenic and inorganic arsenic compounds are a cause of lung cancer. IARC has also identified that there is sufficient evidence to indicate that inorganic arsenic compounds can cause cancer of the urinary bladder and skin.14

Exposure to arsenic

People most commonly exposed to arsenic are those who work in the mining and metal-manufacturing industries.76 Workers in the manufacture of agricultural chemicals, dyestuffs, pharmaceuticals and wood preservatives, and the mining, metallurgical, glass-making and semiconductor industries can also be exposed.14,77

Occupational exposure usually occurs by inhalation of particles that contain arsenic in industrial facilities such as smelters; coal-burning power plants; and battery-assembly, glass-manufacturing and electronics facilities.14 It is possible that people who live near these industrial facilities may be exposed to arsenic in the air.

Arsenic exposure can also occur through contaminated drinking water. This is more common in developing countries, where arsenic contamination of water can be high.14

What is the risk?

Evidence suggests that occupational exposure to arsenic compounds in smelter workers, miners (particularly tin and gold miners) and in production workers increases the risk of developing lung cancer, with an overall risk resulting from occupational exposure to arsenic and its compounds of 1.5–1.7.3

Generally, the greater a person’s cumulative exposure to arsenic, the higher their risk of developing lung cancer, with risk elevated two- to threefold with greater levels of exposure and longer duration of exposure to arsenic i.e. longer duration of employment ranging between 10 and 40 years (relative risk 2.0–3.0).3

Exposure by inhalation

Smelter workers and people living near smelters

Smelter workers may have an increased risk of developing lung cancer from arsenic exposure, although a precise estimate of the risk cannot be calculated because the studies varied in their methods of measuring exposure. Relative risks in most studies increase with exposure to higher levels of arsenic, up to a relative risk of 3.7 (95% CI 2.1–6.4) for smelter workers exposed to high levels for more than 10 years.14

The evidence of lung cancer risk for people living near smelters or other arsenic-producing industrial facilities is inconclusive because of the limited number of studies and mixed results from those studies that are available.15,78
Exposure by inhalation contd.

Other occupational exposures

Studies have investigated the risk of developing lung cancer or dying from lung cancer in production workers at a fertiliser plant, nickel refinery workers, stokers and pesticide manufacturers. Two studies showed that these workers were more likely to develop lung cancer due to their exposure to arsenic than unexposed people.14 The risk of lung cancer increased with increasing duration of employment.14

Effect of smoking

Smoking appears to interact with arsenic exposure to further increase the risk of developing lung cancer, particularly for smelter workers and metal miners.15,16

Exposure by ingestion

The World Health Organization (WHO) recommends that drinking water should not contain more than 0.01 milligrams of arsenic per litre (mg/L). In Australia, prescribed safe levels of arsenic in drinking water are set at a maximum of 0.007 mg/L.76

Based on data from studies conducted in some parts of Japan, Chile and Taiwan, there is evidence that high levels of arsenic in drinking water are associated with an increased risk of lung cancer.14,17 However, these findings are not generalisable to developed countries such as Australia, where concentrations of arsenic in the drinking water are well within the prescribed safety levels.

Effect of smoking

Studies suggest that smoking further increases the risk of lung cancer after exposure to arsenic in drinking water, particularly at high concentrations of arsenic.14
Polycyclic aromatic hydrocarbons (PAHs) are byproducts of burning organic material, such as coal, crude oil, natural gas, garbage and tobacco.\textsuperscript{18,79} PAHs can enter the body through the skin, respiratory tract and digestive tract, where they are slowly absorbed by cells and cause DNA damage, which can contribute to cancer.\textsuperscript{80}

IARC has identified that there is sufficient evidence to indicate that various occupational exposures to PAHs are a cause of lung cancer.\textsuperscript{80,81} As well as lung cancer, IARC identified that these exposures can cause cancer of the bladder and skin.\textsuperscript{80,81}

**Exposure to polycyclic aromatic hydrocarbons**

Sources of PAHs include tobacco smoke, urban and industrial air pollution, and diet. People working in particular occupations and industries may be exposed to high levels of PAHs.\textsuperscript{80} PAH exposure usually includes a mixture of different PAHs, but benzo-a-pyrene (BaP), a common PAH, is often measured as a marker of general PAH exposure.\textsuperscript{18,80}

**What is the risk?**

Evidence suggests that occupational exposure to PAHs in various industries, particularly coal gasification, coke production and potentially aluminium production, increases the risk of developing lung cancer. Overall, increases in risk ranged from 1.2 to 2.3 times for people exposed compared with those not exposed.\textsuperscript{3}

The risk of developing lung cancer due to PAH exposure varies across different industries. For example, one meta-analysis reported that people exposed to PAHs in the coal gasification industry were 2.3 times more likely to develop lung cancer than workers not exposed to PAHs in the industry (relative risk 2.3, 95% CI 2.0–2.6). Similarly, people exposed to PAHs in the coke production industry were 1.6 times more likely to develop lung cancer than unexposed workers (relative risk 1.6, 95% CI 1.5–1.7), while the relative risk for people in the carbon black production industry was 1.3 (95% CI 1.1–1.6).\textsuperscript{18}

Aluminium production workers may also be at increased risk of developing lung cancer from PAH exposure, although the variation in results of reported studies is large. Two studies showed no significant increase in risk;\textsuperscript{18,82} however, analysis of two other large studies\textsuperscript{83,84} showed a relative risk of 2.2 (95% CI 1.5–3.1).\textsuperscript{3} These differences may be attributable to different levels of exposure or different processes in different countries.

There is inconsistent evidence for an association between exposure to PAH and lung cancer for workers employed in coal tar distillation, creosote production, carbon black production and carbon electrode manufacture.\textsuperscript{18} Apparent variations in study results of risk across industries are also affected by limitations of the data, including the small number of studies and the lack of standardised methods to measure exposure.

Studies on cumulative PAH exposure do not show a clear relationship between PAH exposure and the risk of developing lung cancer over time.

The risk of developing lung cancer associated with PAH exposure appears to increase in smokers; however, the evidence is inconclusive because of limitations in the available studies.\textsuperscript{3,83–85}
Cadmium

Cadmium is a metal that occurs naturally in the Earth’s crust and in sea water. It is used in a range of industrial applications, including manufacture of nickel–cadmium batteries, pigments, coatings and plating, stabilisers for plastics, alloys, semiconductors and solar panels. Cadmium is also an impurity in non-iron metals, steel, fossil fuels, cement and phosphate fertilisers.

Cadmium is released into the air from erosion of cadmium-containing rocks, sea spray and bushfires. Industrial sources include mining and smelting zinc, burning fossil fuels, incinerating waste and producing cement. Cadmium does not break down in the environment and can accumulate over time, especially in or near industrial areas.

IARC has identified that there is sufficient evidence to indicate that cadmium is a cause of lung cancer.

Exposure to cadmium

Industries with the highest potential for occupational cadmium exposure include cadmium production and refining, nickel–cadmium battery manufacturing, cadmium pigment manufacturing, cadmium alloy production, mechanical plating, zinc smelting, cadmium–silver alloy soldering, and polyvinyl chloride (PVC) compounding. Occupational exposure to cadmium has decreased since the 1970s, and many countries enforce regulations that restrict its use.

People who do not work with cadmium can be exposed to it through the air, food and contaminated dust. Smoking is also a source of cadmium exposure.

What is the risk?

Overall, the evidence suggests that there is a modest increase in risk of lung cancer associated with cadmium exposure. However, the high level of variability in studies makes it difficult to measure the overall risk of developing lung cancer due to cadmium exposure. There is no clear trend between duration of cadmium exposure and risk of lung cancer; however, one study suggests that the relative risk is up to 2.7 for people exposed to higher levels of cadmium over time (more than 2920 mg/m³-days, a measure of cumulative cadmium exposure over time).

Occupational exposure

In Australia, the risk of harmful cadmium exposure is low. There are guidelines in place to limit industrial emissions of cadmium and to limit cadmium exposure in the workplace.

It is difficult to define the risk of occupational cadmium exposure. Several studies of people who were exposed to cadmium in their occupations for at least one year showed that the risk of developing lung cancer compared with the risk in people who had never been exposed to cadmium, or compared with the general population, appeared to be elevated, but results were not statistically significant. These studies were constrained by the small numbers of workers who had been highly exposed and had worked long term, the lack of historical data on exposure, and difficulties defining and measuring cumulative exposure across studies.

Cadmium fumes or mist contain smaller particles than cadmium dust, which may be more easily absorbed through the lungs. One study suggests that exposure to cadmium fumes or mist at high levels or for a long duration has a higher risk than exposure to cadmium dust (relative risk 2.1, compared with 0.7–1.0 for cadmium dust), although the trend was not statistically significant.

Residential exposure

Because cadmium does not break down in the environment, it can also accumulate in soil, particularly in areas near industrial sources of cadmium. One study of people living in an area of Belgium near three zinc smelters, where there were high levels of cadmium in the soil, found that they were 3.6 times more likely to develop lung cancer than people who lived in unexposed areas (relative risk 3.6, 95% CI 1.0–12.7). It is possible that house dust in these areas acts as a persistent source of cadmium exposure.

Effect of smoking

It is not clear whether smoking interacts with cadmium exposure to affect the risk of lung cancer—some studies show that risk from cadmium exposure increases with smoking, others show that the risk from cadmium exposure is higher for non-smokers. More studies are needed to determine the interaction between cadmium exposure and smoking as a risk of lung cancer.
Asbestos

Asbestos is a naturally occurring mineral. There are six types of asbestos, characterised by the shape of their fibres: the long, narrow chrysotile (white asbestos); the shorter and wider amphibole types—amosite and actinolite (brown asbestos); anthophylite and crocidolite (blue asbestos); and tremolite.22

The health risks of asbestos have been well studied, and there is a substantial body of research on this topic, primarily relating to occupational asbestos exposure. IARC has identified that there is sufficient evidence to indicate that asbestos is a cause of lung cancer.22 As well as lung cancer, IARC has identified that asbestos causes mesothelioma and cancer of the larynx and ovary.22 For the purposes of this evidence overview, mesothelioma is not classified as lung cancer, and studies on mesothelioma are therefore not included.

Exposure to asbestos

Asbestos was commonly used in building materials in the form of asbestos cement, vinyl floor coverings, lagging of pipes and boilers, and insulation. It was used extensively in Australia, particularly between 1945 and 1980, and was also mined in Australia.91 Asbestos was banned from use in building products in Australia in 1989, although it remained in gaskets and brake linings until recently. It was completely prohibited in 2004 and cannot be imported, used or recycled.91 However, it is still present in buildings that were constructed using these materials before the ban.

The risk from asbestos is due to the inhalation of fibres, especially in high doses or over long periods of time. This can occur as part of a person’s occupation (e.g. asbestos miners, manufacturers of asbestos building products, builders), or in other circumstances such as home renovations, where drilling or other activities can release fibres into the air (which can be inhaled) or into a water supply (where they can be ingested in drinking water).

What is the risk?

Research in this overview offers clear indication of an increased risk of lung cancer following exposure to asbestos. Most studies of exposure to asbestos have been undertaken on male populations, most likely because, historically, men have worked more often than women in occupations such as mining and other industries that may be exposed to asbestos.

Occupational exposure to asbestos

There is evidence to suggest that occupational exposure to asbestos increases the risk of developing lung cancer by approximately 1.3–2.0 times.3 Studies have investigated occupations such as asbestos mining, various types of manufacturing, ship building, railway construction and plumbing.

In the manufacturing industry, workers exposed to asbestos generally have a higher risk of developing lung cancer. However, results were variable because of the different ways in which exposure was measured. A meta-analysis of several studies found that manufacturing workers exposed to asbestos are twice as likely to develop lung cancer than workers who have not been exposed (relative risk 2.0, 95% CI 1.7–2.4).3,22 Manufacturing workers at increased risk include insulation workers (relative risk 2.8, 95% CI 2.0–3.9),21 textile workers (2.2, 95% CI 1.8–2.6)3 and cement workers (1.8, 95% CI 1.4–2.4).3 Workers exposed to asbestos in other sectors of manufacturing, including rail workers, shipyard workers and plumbers, also show a significantly elevated risk of lung cancer and are approximately 1.3 times more likely to develop lung cancer than those who have not been exposed (relative risk 1.3, 95% CI 1.1–1.6).1,22 However, results from studies on these workers were variable because of differences in duration, intensity and type of exposure.

Overall, a person’s risk of developing lung cancer starts to increase significantly after approximately 10 years of occupational exposure to asbestos, and this risk increases with increasing duration of exposure.3,22 The length of time between exposure to asbestos and development of lung cancer is usually 20–40 years.91
Non-occupational exposure to asbestos

Results from the three studies on non-occupational exposure to asbestos are variable. Two studies examined people living near asbestos industries: one showed that risk increased with increasing exposure; the other showed no increase in risk.22 A study of residential exposure from asbestos-containing whitewash found that risk increased with more than 20 years of exposure.94 More studies are required on non-occupational exposure to asbestos to clarify the risks.

Asbestosis and lung cancer

Some research has focused on whether asbestosis (a disease in which the lungs become inflamed and scarred as a result of exposure to asbestos) is related to the development of lung cancer. Studies show that the risk of lung cancer in people with asbestosis is higher than in the general population (standardised mortality ratio ranged from 1.7 to 6.2 across different studies),22 and also higher than in people who have been exposed to asbestos but do not have asbestosis.23 However, the evidence also suggests that asbestosis is not necessary for asbestos exposure to present a significant risk of lung cancer.

Effect of smoking

There is evidence from all included studies in the systematic review that smoking (or a history of smoking) compounds the risk of lung cancer in people already at increased risk due to their high exposure to asbestos, and that the relationship between asbestos and smoking in lung cancer is more than additive. One large study from the United Kingdom showed that people who smoked one pack of cigarettes per day for 35 years and had been exposed to asbestos in their jobs for more than 30 years were 26 times more likely to develop lung cancer than people who had never smoked and had been exposed to only low levels of asbestos in their jobs (relative risk 26.2, 95% CI 13.0–53.1).21 The risk was lower for former smokers, but remained highly significant; former smokers (one pack per day for 17 years) exposed to asbestos for more than 30 years were almost 10 times more likely to develop lung cancer than people who had never smoked or been exposed to significant levels of asbestos (relative risk 9.7, 95% CI 4.7–20.0).21 In the same study, never-smokers exposed to asbestos for more than 30 years had a relative risk of developing lung cancer of 1.6 (95% CI 0.6–4.2).21

Type of asbestos fibre

It is not clear whether the type of asbestos fibre affects the risk of developing lung cancer. Many studies include people who have been exposed to multiple types of asbestos, particularly chrysotile and crocidolite, but detailed and accurate exposure characteristics are often unavailable. This makes it difficult to ascertain any differences in the risk of lung cancer, between different types of asbestos fibres. There is evidence, however, that chrysotile and crocidolite miners are at increased risk of developing lung cancer, with a relative risk of between 1.1 and 1.7.3 This evidence suggests that both chrysotile and amphibole fibre types increase the risk of lung cancer. Recent studies suggest that lung cancer may take longer to develop after exposure to chrysotile asbestos than after exposure to amphibole types of asbestos.96,97
Silica

Silica is a term used to describe a group of minerals that contain silicon and oxygen. These minerals are common in nature, and silica is found in almost all types of rock, clay, gravel and sand, as well as in construction materials such as concrete, bricks and tiles. Silica exists in two forms: crystalline and amorphous.

Inhaled crystalline silica resulting from occupational exposure has been identified by IARC to increase the risk of lung cancer. Its ability to cause cancer depends on the characteristics of the silica, and on other factors that might affect the way it interacts with a person's body.

Exposure to silica

Crystalline silica can form dust particles that are small enough to be inhaled. Exposure to silica can occur in a person's occupation, particularly in industries such as founding, pottery, sandblasting, construction, quarrying, and clay and glass manufacturing and processing.

What is the risk?

The relative risk of developing lung cancer in people exposed to silica is similar across a range of occupations. Studies show that people exposed to silica in mining, quarrying, and the granite, ceramic, steel and industries are approximately 1.2–1.3 times more likely to develop lung cancer than people who are not exposed.

Combined data from people exposed to silica in the mining industry (lead, zinc, gold and copper) show they have a relative risk of developing lung cancer of approximately 1.2 (95% CI 1.0–1.4), although different studies collected data in different ways, and study participants were exposed to varying levels of silica in different types of mines.

Increased risk of lung cancer is also shown for industrial workers in ceramics (relative risk 1.2, 95% CI 1.1–1.4) and diatomaceous earth industry (relative risk 1.4, 95% CI 1.1–1.9).

Studies suggest that the risk of developing lung cancer is affected by the duration of silica exposure. One study found that the risk of lung cancer did not increase to a statistically significant extent until people had been exposed to silica for 26–51 years, leading to a relative risk of 1.7 (95% CI 1.1–2.4).

The intensity of exposure (how much silica a person is exposed to) also increases the risk—people with a cumulative exposure of 1 mg/m³/year have a relative risk of 1.2, and this increases to 1.8 with a cumulative exposure of 6 mg/m³/year.

Risk of lung cancer in people with silicosis

Silicosis is a disease that causes scarring of the lungs. It is caused by repeated and prolonged exposure to silica. People with silicosis are approximately twice as likely to develop lung cancer as people who are exposed to silica but do not have silicosis (relative risk 2.0).

Effect of smoking

People who smoke and are exposed to silica have a higher risk of developing lung cancer than non-smokers who are exposed to silica. This risk increases the more a person smokes, and the more silica they are exposed to.

Results from an analysis of two Canadian studies examining the joint effects of silica exposure and smoking showed that all categories of smoker are associated with increased risk of lung cancer. For any level of silica exposure, the relative risk of developing lung cancer is 3.2 (95% CI 1.5–6.8) for people who have smoked one pack of cigarettes per day for less than 20 years. The relative risk increases to 6.8 (95% CI 4.0–11.4) for people who have smoked one pack of cigarettes per day for 20–50 years, and up to 23.2 (95% CI 14.4–37.4) for people who have smoked one pack of cigarettes per day for more than 50 years. In the same study, the relative risk of lung cancer due to silica exposure in non-smokers was 1.3 (95% CI 0.5–3.2). The relative risks for both smokers and non-smokers were higher for ‘substantial’ silica exposure (although this level of exposure was not well defined).
Iron and steel founding

Founding is the process of pouring molten metal or glass into a mould to create a new shape or object. Iron and steel foundries make parts for machinery, motor vehicles, railway engines, stoves and wheels. Workers in this occupation may be exposed to several risk factors for lung cancer, such as asbestos, polycyclic aromatic hydrocarbons, silica, chromium, nickel and cadmium.\textsuperscript{32}

IARC has identified that there is sufficient evidence to indicate that occupational exposures during iron and steel founding are a cause of lung cancer.\textsuperscript{99}

Exposure to iron and steel founding

People who work in the production processes of iron and steel founding can be exposed to several risk factors for lung cancer.\textsuperscript{32} People who work in office or administrative roles at foundries are unlikely to be exposed and are not at increased risk of developing lung cancer.\textsuperscript{32}

What is the risk?

Overall, evidence suggests that iron and steel foundry workers are 1.3–1.4 times more likely to develop lung cancer than people who do not work at foundries.\textsuperscript{3,18} Two studies examined the risks associated with different jobs within a foundry. Results of these studies showed that those workers at the industrial site engaged in production showed an increased risk of lung cancer compared with the general population, while office workers at the industrial site did not.

Exploring particular roles, one study showed that only blast furnace workers had a significantly higher risk of lung cancer (odds ratio 2.6, 95% CI 1.3–5.2), and no significant elevation in risk was found for workers in coke batteries, steel mills, lamination facilities, steel foundries, maintenance furnaces or facilities producing coke byproducts.\textsuperscript{32,33} Further research on these individual studies is required to align risk of lung cancer with specific roles in the industry with any certainty.

There is insufficient evidence to determine how each of the individual risk factors associated with foundries contributes to the overall risk of lung cancer; however, one study found that foundry workers exposed to silica had a significantly higher risk of lung cancer.\textsuperscript{100}

The longer a person is exposed to iron or steel founding, the higher their risk of lung cancer. An analysis of studies showed that people who had worked in the industry for less than 10 years did not have a higher risk of developing lung cancer, but people who had worked in iron and steel founding for more than 30 years were 1.9 times more likely to develop lung cancer than people who do not work in the industry (relative risk 1.9, 95% CI 1.1–3.1).\textsuperscript{3}

Effect of smoking

Studies of iron and steel founding and smoking indicate that foundry workers who smoke are at a higher risk of developing lung cancer than foundry workers who do not smoke, and the risk increases with increased smoking.\textsuperscript{33–35} However, the extent of risk varies significantly among studies: for the highest category of smoking, relative risks ranged from 2.8\textsuperscript{35} to 118.1.\textsuperscript{33} The studies also measured the amount of smoking in different ways, preventing meta-analysis of the results.
Nickel

Nickel and its compounds are naturally present in the Earth’s crust. They can be released into the air by natural processes such as windblown dust, volcanic eruptions and bushfires, or through human activities such as mining, smelting, refining, manufacturing, burning fossil fuels and burning waste. Nickel is often combined with other metals to form alloys that are used in stainless steel, electroplating, coinage, catalysts and welding components. Nickel can accumulate in the lungs, interfering with cells of the immune system and damaging DNA, which can contribute to cancer.

IARC has identified that there is sufficient evidence that nickel compounds and nickel metal are a cause of lung cancer. Nickel compounds and nickel metal also cause cancers of the nasal cavity and paranasal sinuses.

Exposure to nickel

Nickel can be inhaled, ingested through food or drinking water, or absorbed through the skin. Most people are exposed to nickel in the air and in food, but this level of exposure is not considered to be a risk. People who work with nickel in their jobs can be exposed to higher levels of nickel through fumes, dust and mist.

All the included studies investigated occupational exposure of male workers to various forms of nickel.

What is the risk?

Evidence suggests that occupational exposure to nickel represents a significant, but modest, increase in the risk of lung cancer. The variability in studies included in the systematic review makes it difficult to provide a clear, quantifiable risk. However, the studies are consistent in the risk they demonstrate. The majority of research informing the systematic review was conducted in Europe, with no included studies conducted in Australia.

Two pooled analyses show that people who are exposed to nickel in their jobs are approximately 1.3 times more likely to develop lung cancer than people who are not exposed to nickel. A study in Norway showed that work in a nickel refinery for more than one year significantly increased the risk of lung cancer for smelter workers (odds ratio 2.7, 95% CI 2.1–3.6), roasters (odds ratio 3.4, 95% CI 2.3–4.8) and nickel electrolysis workers (odds ratio 4.0, 95% CI 3.3–4.8) compared with other Norwegian men.

The risk of developing lung cancer due to nickel exposure appears to increase with increasing duration of exposure. Evidence from a pooled analysis of two studies in a Canadian nickel refinery found that the risk of lung cancer was only significant for workers who had been exposed to nickel for more than 20 years (relative risk 1.6, 95% CI 1.1–2.3).

The amount of nickel exposure over time also appears to affect the risk of developing lung cancer. In particular, exposure to high levels of water-soluble nickel was found in two studies to increase the relative risk to approximately 3.1 (95% CI 1.7–5.5) compared with people who are not exposed to nickel. The two studies that measured cumulative exposure used different amounts for the highest exposure category, but the trend of increased risk was the same in both studies.
Type of nickel compound

One study examining the type of nickel compound and lung cancer risk found that exposure to water-soluble nickel, nickel oxide, nickel sulfide and metallic nickel all increased the risk of lung cancer, compared with the general population of men in Norway.105 At low exposure (cumulative exposures of 0.01–0.05 mg/m³ over time, depending on the compound), risks (odds ratios) ranged from 1.3 to 1.7. Nickel sulfide became a significant risk at lower concentrations than other compounds, and water-soluble nickel had the highest risk at the highest concentrations.105

Effect of smoking

Smokers who are exposed to nickel appear to have a higher risk of developing lung cancer than non-smokers who are exposed to nickel, and this risk increases with increasing nickel exposure. In one study, nickel refinery workers exposed to less than 1 g/m³ of nickel per year who have ever smoked were 5.6 times more likely to develop lung cancer than non-smoking nickel refinery workers (relative risk 5.6, 95% CI 2.0–15.0).37 Workers exposed to more than 1 g/m³ of nickel per year who have ever smoked were approximately 9 times more likely to develop lung cancer than workers who had never smoked (relative risk 9.1, 95% CI 3.4–25.0).37 However, there was considerable variability in the results of studies examining the effect of smoking in people exposed to nickel.
Beryllium

Beryllium is a naturally occurring metal that is found in rocks, coal, oil, volcanic dust and soil.107 It is mostly used in the nuclear and aerospace industries to make precision instruments and structures, as well as high-speed computers and audio components.107,108 In Australia, beryllium is mainly used in small quantities in electronic components.42 It can also be part of emissions from fossil fuels, such as coal-fired power stations.42

IARC has identified that there is sufficient evidence to indicate that beryllium and its compounds are a cause of lung cancer.109 However, not all forms of beryllium are thought to be equally toxic, and further research is required to fully understand the health effects of beryllium exposure.42

Exposure to beryllium

Beryllium can be inhaled or ingested. Ingesting beryllium is not associated with harmful effects because very little of it is absorbed through the gastrointestinal tract, but inhaling beryllium can irritate the eyes, skin and respiratory tract, and inflame the lungs. Inhaling beryllium can cause acute beryllium disease, which has symptoms similar to pneumonia and can be fatal.42,109

Exposure to beryllium can be an occupational risk in some specialised workplaces such as mining and processing beryllium ores, manufacturing and processing beryllium alloys or compounds, or working with metals that contain beryllium.42 However, relatively high levels of beryllium exposure are required to increase risk of lung cancer.42 In Australia today, it is unlikely that workers or people in their domestic environments would be exposed to beryllium at levels that may increase the risk of lung cancer.42

What is the risk?

Evidence suggests that occupational exposure to beryllium represents a modest risk factor for lung cancer, and any risk is dependent on a relatively high level of exposure. All the studies on beryllium exposure included in the systematic review have been of men who worked in beryllium processing plants in the United States for at least two days between 1940 and 1970. The generalisability of results outside this cohort is uncertain.

Overall, the relative risk of developing lung cancer in these men is 1.0–1.2, but this varied among processing plants. In the plants with high levels of exposure, the relative risk was approximately 1.4–1.5 compared with non-exposed workers.38-41 It is unlikely that, in Australia today, workers would be exposed to beryllium at levels that may present an increased risk of lung cancer.

The type of beryllium may also affect the risk of developing lung cancer. The results of one small study suggest that exposure to different types of beryllium may present different levels of lung cancer risk.41 However, the evidence in this regard, being from one small study, is too scant to draw any firm conclusion on lung cancer risks.

The studies included in the systematic review indicate that only at relatively high occupational exposures is there an elevated risk of lung cancer associated with beryllium exposure. Results from the US studies suggest that low exposure, even at levels equivalent to average exposure in industry, does not represent a significant risk of lung cancer.1

No evidence was identified that demonstrated an effect of smoking on the risk of lung cancer in people exposed to beryllium.
Painting as an occupation

More than 41 000 people are employed as painters in Australia. These workers use paints, varnishes and stains to protect or change the appearance of buildings and structures. Paint contains a range of pigments, binders, solvents and other additives, which differ depending on the desired properties of the paint.

IARC has identified that there is sufficient evidence to indicate that occupational exposure as a painter is a cause of lung cancer. IARC has also identified that there is sufficient evidence to indicate that occupational exposure as a painter is a cause of mesothelioma and cancer of the bladder. Spray painting is thought to be more hazardous than non-spray painting because the paint is sprayed into fine particles that can be inhaled easily. Workers in the painting trade may also be exposed to other risk factors for lung cancer, such as asbestos, chromium and cadmium.

Exposure to paint

People who work with paint every day in their occupation have much higher exposure than people who do not work as painters. Most studies on painting as an occupation used a person’s job title or classification as the measure of exposure, rather than actual exposure to particular paints, environments or other factors; this makes it difficult to determine the precise aspects of painting as an occupation that can increase risk.

What is the risk?

The research identified and synthesised in the systematic review suggests that occupational exposure to paint represents a modest risk factor for lung cancer. The combined results of several studies show that, overall, people who work as painters are 1.3 times more likely to develop lung cancer than people who do not work as painters. One study found that painters in the construction industry have a risk (odds ratio) of 1.6 (95% CI 1.0–3.1) compared with non-painters. This may be due to their exposure to other risk factors such as asbestos or silica.

There was inconsistency in the evidence regarding the impact of duration of employment as a painter or a spray painter on lung cancer risk.

No evidence was identified that demonstrated an effect of smoking on the risk of lung cancer in painters.
Chromium is a natural chemical that occurs in two forms—chromium III, which is non-toxic, and chromium VI. Chromium compounds are used in bricks, linings for furnaces, chrome plating, dye manufacture, wood and water treatment, galvanising, printing, paints, degreasers and rust converters. Chromium can be breathed in or ingested through contaminated food or water, where it is absorbed into the body. Once inside the body’s cells, chromium VI breaks down, forming reactive chemicals that can damage DNA and contribute to cancer.

IARC has identified that there is sufficient evidence to indicate that chromium VI compounds are a cause of lung cancer.

Exposure to chromium VI can occur in occupations that involve the production, use and welding of chromium-containing alloys (such as stainless steel and high-chromium steel); the production and use of chromium-containing paints (such as in the aerospace, construction and maritime industries); electroplating; catalysts; chromic acid and pesticides. People who are exposed to chromium VI may also be exposed to other risk factors for lung cancer in their workplaces, and this makes the risk due to chromium difficult to measure. Chromium VI is also present in tobacco smoke.

What is the risk?

Exposure to chromium VI may increase the risk of lung cancer. Combined results of many studies indicate that people who are exposed to chromium VI are at approximately 1.2 times greater risk of lung cancer than people who are not exposed (standardised mortality ratio 1.2, 95% CI 1.1–1.3). Other studies show mixed results, although the trend shows a likely increased risk of lung cancer. However, the risk estimates for many studies are not precise, and relevant details about the people involved in the studies are lacking.

There is insufficient evidence to determine whether duration of exposure to chromium VI affects the risk of developing lung cancer. A study in aircraft manufacturing workers found that people who had been exposed to chromium VI for up to 10 years had a relative risk of lung cancer of 1.2 (95% CI 1.1–1.4); another study found that people exposed to chromium dust for more than 20 years had a relative risk of 1.5 (1.0–2.3) compared with unexposed workers. However, three other studies showed no significant increase in risk, even after adjusting for the amount of exposure over time.

The amount of chromium exposure may have a greater effect on risk than the length of time a person is exposed. One study measured the amount of chromium in people’s urine to determine their occupational chromium exposure. People with less than 200 grams per litre-years (g/L-year, a measure of the concentration of chromium in urine multiplied by the number of years of exposure) did not have an increased risk of lung cancer, even 20 years after they had been exposed to chromium. However, people with urinary chromium levels of more than 200 g/L-year had a twofold greater risk of lung cancer, regardless of how much time had passed since they were exposed.

No evidence was identified that demonstrated the effect of smoking on the risk of lung cancer in people exposed to chromium VI.
Air pollution

This section of the overview focuses on air pollution in the outside air, including gases and particles that comprise urban pollution, and pollution from vehicle exhaust. It does not include indoor air pollution. Air pollution can include chemicals such as sulfur dioxide, nitrogen dioxide and nitrogen oxides, and a range of particles known as particulate matter (PM). PM is classified according to the size of the particles: inhalable (particles 10 micrometres [μm] or less in diameter, also known as PM10), fine (particles 2.5 μm or less in diameter; PM2.5) and ultrafine (particles 0.1 μm or less in diameter; PM0.1).

Exposure to air pollution

The level of air pollution in Australia compares favourably with many other countries: the average PM2.5 level over six years is 12 micrograms (μg) of particles per cubic metre of air (μg/m3).119 The global average is 27 μg/m3, and some areas report more than 100 μg/m3.119 As very high levels of pollution are not comparable to conditions in Australia, studies in these areas (e.g. China) were not included in the systematic review.3

People living in urban and industrial areas may be exposed to more air pollution than those living in rural areas.

What is the risk?

There is evidence that exposure to fine particulate matter (PM2.5) in air pollution increases the risk of lung cancer. Studies in the United States and Europe have estimated relative risks of lung cancer for people who are exposed to fine particulate matter (PM2.5) in air pollution of 1.2–1.3 compared with people who are not exposed to similar levels of PM2.5.49,50 For example, people who are exposed to 10 μg/m3 of PM2.5 for one year are 1.2 times more likely to develop lung cancer than people who have not been exposed to such levels of pollution (relative risk 1.2, 95% CI 1.1–1.3).49 The risk of developing lung cancer from cumulative exposure to fine particulate matter does not appear to increase over time—one study reported that the relative risk after 21 years’ exposure is not significantly different from the risk after one year’s exposure.50

Sulfur dioxide and nitrogen dioxide, which are gaseous components of air pollution, do not appear to increase the risk of lung cancer.40,51 However, there is mixed evidence as to whether other nitrogen oxides are associated with a small increase in risk of lung cancer (relative risk 1.1, 95% CI 1.0–1.2).49,52

None of the included studies reported an increase in lung cancer risk as a result of living near busy or major roads.49,51,52

Limited evidence was available on the effect of smoking on the risk of lung cancer related to air pollution. Results from a single study reported no increased risk of lung cancer as a result of smoking in people exposed to air pollution.51

Diesel exhaust as a risk factor for lung cancer

In June 2012, the International Agency for Research on Cancer (IARC) identified that there is sufficient evidence that exposure to diesel engine exhaust is associated with an increased risk of lung cancer.54 While large populations are exposed to diesel exhaust in everyday life, whether as part of their occupation or through exposure to motor vehicle and other diesel engine exhausts in the ambient air, the main studies that led to IARC’s conclusion were in highly exposed workers. Exposure to diesel exhaust is not included as a risk factor in this overview, as the systematic review was conducted before IARC’s classification of diesel engine exhaust as a substance with sufficient evidence to be causally associated with lung cancer.
Family history

A person's family history can be useful in assessing their risk of developing cancer. Some types of cancer are linked to particular genes, so if one family member—particularly a first-degree relative, such as a parent or sibling—has that type of cancer, it may indicate that other members of the family are at increased risk.

Lung cancer is usually associated with environmental rather than genetic triggers. However, because families share environmental and behavioural characteristics as well as genetic traits, knowledge of a person's family history of lung cancer can help to increase understanding of shared risks. Although research is increasing on genetic factors associated with lung cancer, such as particular enzymes or protein profiles, the systematic review on which this overview is based investigated studies on family relationships only.

Family history can include both modifiable (environmental, behavioural) and non-modifiable (genetic) risk factors.

What is the risk?

There is evidence to suggest that a person who has a family member with lung cancer is approximately twice as likely to develop lung cancer as someone without a family history of the disease (relative risk 2.0). The risk appears to be most significant if two or more family members had lung cancer (odds ratio 3.6, 95% CI 1.6–8.3), and if a person's mother had lung cancer (odds ratio 2.2, 95% CI 1.3–4.0).

People with a family history of lung cancer are more likely to smoke than people without a family history. Smokers who had a family member with lung cancer were at increased risk relative to those who did not smoke.

The role(s) of modifiable factors (such as shared environment) and non-modifiable factors (such as genes) in the association between family history and increased risk of lung cancer is unclear. Research into non-modifiable risk factors is now moving towards studies of genomics, where genetic variations that predispose to lung cancer are being identified, described and quantified.
Factors with limited evidence of an association with lung cancer

Consumption of red meat and processed meat

Red meat (such as beef and lamb) and processed meat (such as cured meats, sausage, ham and bacon) contain salt, saturated fats and some compounds that may contribute to cancer.120 Grilling or barbecuing red meat can also release polycyclic aromatic hydrocarbons,121 which are a risk factor for lung cancer.80,81

Australians consume approximately 87.4 kilograms (kg) of red meat per person per year, or 239 grams (g) per person per day.122 However, some people eat no red meat, and others may eat more than this amount.

Studies of red meat and processed meat

Red meat

Evidence suggests that people who eat large amounts of red meat may be at increased risk of developing lung cancer compared with people who eat little or no red meat (relative risk 1.1, 95% CI 1.1–1.2).3 However, this conclusion should be interpreted with caution, as studies varied in the way they measured lung cancer risk in people who ate large quantities of red meat and in the way that red meat consumption was categorised—the lowest exposure category was usually people who ate no red meat or less than 10 g per day, while the highest category ranged from more than 80 g per day123 to more than nine serves per week.124 Overall, this result is based on approximately 5–10 portions per week; however, portion size across studies was variable. None of the studies investigated whether the method of cooking the meat affected risk.

The effect of duration of exposure to large amounts of red meat on the risk of developing lung cancer is not clear. Most studies used questionnaires to evaluate people’s meat intake; some of these asked people about their usual diet over the past 2–5 years, but others did not account for duration of exposure.

Processed meat

Consumption of large amounts of processed meat also appeared to increase risk of lung cancer by a similar small amount. A meta-analysis of nine studies suggests that people who eat large amounts of processed meat are approximately 1.2 times more likely to develop lung cancer than people who eat little or no processed meat (relative risk 1.2, 95% CI 1.0–1.3).3 However, this conclusion should be interpreted with caution, as studies varied in their definitions of ‘processed meat’ and in their categories of consumption (the lowest category was no serves of processed meat or less than 10 g per day; the highest category varied but was less than for red meat consumption). The method of processing (e.g. salting, smoking) and whether the meat was raw or cooked also varied across studies.

The effect of duration of exposure to large amounts of processed meat on the risk of developing lung cancer is not clear.

The effect of smoking on the risk of developing lung cancer from red meat or processed meat consumption is unclear. Two studies suggested that smoking increased the risk of lung cancer in men and women who ate large amounts of red meat.124,125 However, the wide confidence intervals (especially for women) make it difficult to determine the exact increase in risk. A single study in men who ate more than 4.6 serves of processed meat per week found that former smokers, but not current smokers, were almost twice as likely to develop lung cancer due to high processed meat consumption as men who ate little or no processed meat (odds ratio 1.9, 95% CI 1.1–3.1).125 However, more studies are required to further investigate this risk.
Alcohol consumption

Approximately 8.9% of Australians over the age of 14 years drink alcohol on a daily basis.126 Men consume more alcohol than women: 12% of men drink alcohol daily, and 48% drink alcohol weekly, compared with 6% and 35% of women, respectively.126

IARC has identified that there are inadequate data to indicate that alcohol consumption is a cause of lung cancer.127 However, IARC has identified that there is sufficient evidence to indicate that alcohol consumption causes cancers of the oral cavity, pharynx, larynx, oesophagus, colorectum, liver (hepatocellular carcinoma) and breast.128

Studies of alcohol consumption

The studies examined in the systematic review suggest that alcohol consumption does not independently increase the risk of lung cancer.3 However, studies varied in focus and measured alcohol consumption in different ways, and not all of them adjusted for smoking.

Some studies found an increased risk of lung cancer with high alcohol consumption (more than five drinks per day),129,130 but other studies found no significant association between any level of drinking and lung cancer.131-134

There are no clear data in the studies of lung cancer effects by duration of exposure to a particular level of alcohol consumption. The length of follow-up in these studies ranged from 7 to 17 years.

Some studies suggest that smoking may interact with alcohol consumption to increase the risk of lung cancer.135-137

Dietary and blood cholesterol

Cholesterol is important for healthy cell function, but excess cholesterol can be harmful. Cholesterol is found in many foods, and dietary cholesterol intake affects the amount of cholesterol that circulates in a person's blood. It is estimated that every 100 g of cholesterol consumed in a person's diet raises their blood cholesterol by 2–3%.138

Different foods contain different levels of cholesterol; therefore, exposure depends on diet. Foods that are high in fat, such as fast food, butter and eggs, are often associated with high levels of cholesterol, while fresh fruit and vegetables contain little cholesterol.

IARC has identified that the evidence is inadequate to indicate whether dietary cholesterol is a cause of lung cancer.139

Studies of dietary and blood cholesterol

Studies included in the systematic review measured cholesterol intake in several different ways, but this was usually per day or per week, with no indication of the length of time (e.g. number of years) a person had been consuming that level of cholesterol in their diet.3

Dietary cholesterol

While studies of dietary cholesterol and risk of lung cancer have mixed results, overall the evidence suggests that dietary cholesterol intake does not increase the risk of developing lung cancer. Some studies found no association between the amount of cholesterol in a person's diet and their risk of lung cancer,140,141 while others found relative risks of up to approximately 1.6 for people with high-cholesterol diets.142,143

A large pooled analysis showed no interaction between smoking, dietary cholesterol and risk of lung cancer.141

Blood cholesterol

High blood cholesterol does not appear to impart any risk of lung cancer on individuals. Rather, the evidence suggests that high blood cholesterol may have a modest protective effect and reduce the risk of lung cancer.

Conversely, if plasma cholesterol concentrations are low (<160 milligrams per decilitre), there is some evidence to suggest that the risk of lung cancer is increased.144-147 However, this does not suggest that low cholesterol is a risk factor for lung cancer—it is more plausible that this is a non-causal correlation.
Exposure to birds

The potential for pet birds to increase indoor air pollution and spread disease has led to research into their association with various diseases, including lung cancer. Pet birds can be kept either inside the house or outdoors in an aviary or similar enclosure. Exposure to birds can also occur in a person’s occupation (e.g. aviary worker, zookeeper) but no studies identified have investigated the risk of developing lung cancer from occupational exposure to birds.

Studies of exposure to birds

While studies on exposure to birds and risk of lung cancer have mixed results, combining the results of several studies suggests that exposure to birds does not increase the risk of lung cancer overall. Three of four studies found no association between the lengths of time that people were exposed to birds and their risk of lung cancer. Studies suggest that smoking does not affect the risk of lung cancer from exposure to birds.

Exposure to wood dust

Wood dust can be present at high levels in industries that work with forestry products, such as furniture factories, pulp mills and paper mills, as well as in woodworking as a hobby. Manipulation of wood, such as drilling and sawing, can create fine dust particles that can be inhaled. Exposure to wood dust usually occurs as part of a person’s occupation.

Studies of wood dust

It is difficult to measure the duration and intensity of exposure to wood dust, and this makes it difficult to determine its effect on lung cancer risk. Also, people who are exposed to wood dust (particularly in the workplace) may also be exposed to other risk factors for lung cancer, such as asbestos or other types of dust, which can confound results.

People who are exposed to wood dust are not likely to have a higher risk of developing lung cancer than people who are not exposed. Four studies found no association between wood dust exposure and lung cancer, and two studies found small increases in risk. These small increases were found only after approximately 20 years of exposure to wood dust, suggesting that increased risk may be apparent for long duration of exposure.

Almost all the studies included men only, and none of the studies looked at the effect of smoking on risk of lung cancer after wood dust exposure.
Physical activity

Physical activity is associated with daily living, work and leisure activities, and is considered to be beneficial for health and the prevention of chronic diseases.

Studies of physical activity

Increased physical activity is not associated with an increased risk of lung cancer but may rather reduce the risk of the disease.

A research synthesis and six research studies have been included in the systematic review to investigate the association between physical activity and risk of lung cancer, with most, but not all, suggesting an inverse association between higher levels of physical activity and lung cancer risk. The findings presented in each study included in the systematic review varied in terms of type, frequency and duration of physical activity, amount of energy expended and intensity of physical activity, precluding an overall assessment of risk reduction. In addition, limitations of these studies included the influence of factors outside the control of the investigators, such as subjective interpretation of questionnaires.

Most studies, however, suggest that people who participate in some physical activity may be at a reduced risk of developing lung cancer when compared to those who are physically inactive.

Refer to the National Physical Activity Guidelines for current Australian recommendations for physical activity.
## Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tr>
<td>Absolute risk</td>
<td>A person’s chance of developing a disease over a particular period of time. It is calculated by dividing the number of people who have the disease in a particular group by the total number of people in that group.</td>
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<tr>
<td>Active smoking</td>
<td>Smoking tobacco through any means, including cigarettes, cigars, pipes, bidis and waterpipes. It does not include exposure to other people’s tobacco smoke (see Passive smoking).</td>
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<tr>
<td>Becquerel</td>
<td>The SI unit of radioactivity.</td>
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<tr>
<td>Confidence interval (CI)</td>
<td>A measure of the precision of the risk estimate—the narrower the interval, the more precise the estimate of the risk, and the less likely that the risk would be subject to chance variation. A 95% CI indicates that we are 95% certain that the true value of the estimate lies within that range.</td>
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<tr>
<td>Incidence</td>
<td>The number of new cases of an illness that occur during a given period in a specified population.</td>
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<tr>
<td>Level of evidence</td>
<td>An indication of the quality of the evidence, based on the likelihood of the study results being affected by bias. In this overview, levels of evidence range from Level I (high quality, low level of bias) to Level IV (lower quality, higher likelihood of bias).</td>
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<tr>
<td>Lung cancer</td>
<td>Uncontrolled growth of cells in the lung. Different types of lung cancer originate in different types of lung cells, and include small cell carcinoma, non–small cell carcinoma and other types. Cancers that originate in other parts of the body can spread to the lungs and cause secondary cancers; however, this overview only considers primary lung cancer.</td>
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<tr>
<td>Mesothelioma</td>
<td>Cancer of the lining of the chest and abdominal cavities. Pleural mesothelioma is a type of cancer affecting the membrane (the pleura) that covers and protects the lungs. Mesothelioma is not a primary lung cancer, so is not included in this overview.</td>
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<tr>
<td>Odds ratio</td>
<td>A measure of the association between an exposure and an outcome. It describes the odds that an outcome (e.g. lung cancer) will occur after exposure (to a certain risk factor), compared with the odds of the outcome occurring without the exposure. In rare diseases such as lung cancer, odds ratios can be interpreted as equivalent to relative risks.</td>
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<tr>
<td>Passive smoking</td>
<td>When tobacco smoke (including the smoke released from a burning tobacco product and the exhaled smoke from the person smoking) is inhaled by a person other than through active smoking (i.e. exposure to other people’s tobacco smoke). Also known as involuntary smoking, exposure to environmental tobacco smoke or second-hand smoke, and tobacco smoke pollution.</td>
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<tr>
<td>Primary cancer</td>
<td>A tumour that is at the site where it first formed (see also Secondary cancer).</td>
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<tr>
<td>Relative risk</td>
<td>A person’s chance of developing a disease over a particular period of time relative to another person’s chance of developing the disease. It is calculated by dividing the absolute risk of a group of people who are exposed to a risk factor by the absolute risk of a group of people who are not exposed to the risk factor. Relative risk indicates how many times more likely a person in the exposed group is to develop the disease.</td>
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<tr>
<td>Risk factor</td>
<td>Any factor that is associated with a greater risk of a health disorder or other unwanted condition or event. Some risk factors are regarded as causes of disease; others are not causative. Some risk factors can be modified; others cannot.</td>
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<tr>
<td>Secondary cancer</td>
<td>A tumour that originated from a cancer elsewhere in the body.</td>
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<td>Term</td>
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<tr>
<td>Standardised mortality ratio</td>
<td>The ratio of deaths in the study population to those in the reference population, adjusted for age. For example, a standardised mortality ratio of 1.5 indicates that there were 50% more deaths in the study population.</td>
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<tr>
<td>Statistical significance</td>
<td>An indication from a statistical test that an observed difference or association may be significant or ‘real’ because it is unlikely to be due just to chance. A statistical result is usually said to be significant if it would occur by chance only once in 20 times or less often.</td>
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<tr>
<td>Systematic review</td>
<td>An assessment of published studies that uses rigorous, standardised methods for searching for, selecting, critically appraising and synthesising articles to answer a defined research question. This minimises bias and provides a high level of evidence. See also Level of evidence.</td>
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Appendix 1  International Agency for Research on Cancer (IARC)

The IARC monographs\(^1\) identify factors that can increase the risk of human cancer. Interdisciplinary working groups of expert scientists review the published studies and evaluate the weight of the evidence that an agent can increase risk of cancer. Agents are then categorised as carcinogenic, probably or possibly carcinogenic, or not carcinogenic to humans, based on the strength of the evidence.

The evidence relevant to carcinogenicity of agents from studies in humans is classified into four categories by the IARC Working Group:

- **Sufficient evidence of carcinogenicity (highest IARC classification for carcinogenicity):** The Working Group considers that a causal relationship has been established between exposure to the agent and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence.

- **Limited evidence of carcinogenicity (positive association):** A positive association has been observed between exposure to the agent and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

- **Inadequate evidence of carcinogenicity:** The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available.

- **Evidence suggesting lack of carcinogenicity:** There are several adequate studies covering the full range of levels of exposure that humans are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent and any studied cancer at any observed level of exposure.

The IARC Working Group also considers the body of evidence as a whole, in order to reach an overall evaluation of the carcinogenicity of the agent to humans. The categorisation of an agent into one of the following four groups is a matter of scientific judgment that reflects the strength of the evidence derived from studies in humans and experimental animals, and from mechanistic and other relevant data:

- **Group 1 carcinogen:** The agent is carcinogenic to humans. This category is used when there is sufficient evidence of carcinogenicity in humans.

- **Group 2:** Group 2A (probably carcinogenic to humans) or Group 2B (possibly carcinogenic to humans). This category includes agents for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals.

- **Group 3:** The agent is not classifiable as to its carcinogenicity to humans. This category is used most commonly for agents for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals.

- **Group 4:** The agent is probably not carcinogenic to humans. This category is used for agents for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals.

\(^1\) http://monographs.iarc.fr/index.php
References


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