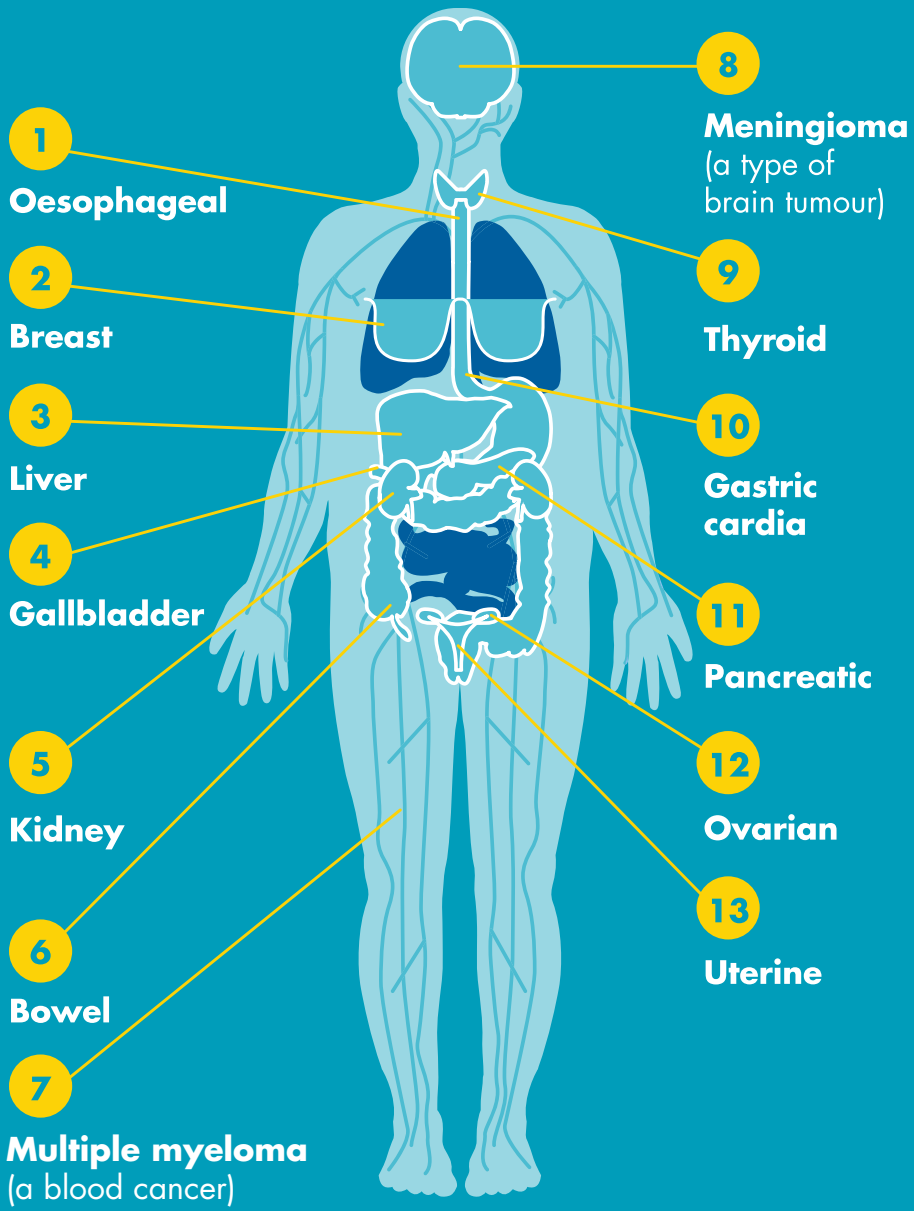
Obesity and increased cancer risk.

A guide for health professionals

In Australia, obesity, poor diet and lack of physical activity are the most important modifiable risk factors for cancer after tobacco and UV exposure.[1]

It is now recognised that overweight and obesity can increase the risk for 13 types of cancer.[2]



Partner:

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Department of **Health**

Cancer Council WA

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Obesity and cancer risk: proposed mechanisms

The relationship between obesity and cancer risk is complex and not fully understood. Despite this, there is strong evidence that overweight or obesity are risk factors for some cancers.[2-4] Obesity is associated with many of the hallmarks of cancer, those features of cancer cells which distinguish them from normal cells: deregulating cellular energetics, sustaining proliferative signalling, avoiding immune destruction, inducing angiogenesis and resisting cell death (apoptosis).[3]

Some of the proposed mechanisms of the obesity–cancer link are described below.

Low level inflammation

Inflammation is a key feature of obesity-related adipose tissue dysfunction and is thought to be an important link between obesity and cancer.

Inflamed adipose tissue resembles chronically injured tissue and can stimulate the same wound healing mechanisms resulting in the generation of a pro-neoplastic microenvironment,[5] for example, immune cell infiltration, production of pro-inflammatory mediators and growth factors, tissue remodelling and angiogenesis.

Once established, tumour cells may co-opt the inflammatory mechanisms responsible for tissue healing and instead promote tumour growth and invasion.[5]

Chronic inflammation is associated with increased cell proliferation and differentiation; decreased apoptosis, and increased angiogenesis all of which contribute to carcinogenesis.[3,4,6]

Alterations to endocrine hormones

Obesity is associated with increased levels of oestradiol due to aromatase in adipocytes converting androstenedione to oestradiol and testosterone.[7] Studies have shown that endogenous sex steroids are strongly associated with post-menopausal breast and endometrial cancer risk. The proliferative effect of oestrogen on epithelial tissue in the breast and endometrium is believed to be an underlying mechanism.[8,9] In addition to this, increased levels of oestradiol may contribute to genome instability.[3]

Alterations to other hormones

Insulin and insulin-like growth factor-1

Obesity is associated with elevated levels of insulin and insulin-like growth factor-1. These hormones are thought to play a role in cancer development by inhibiting apoptosis, contributing to genome instability and stimulating cell proliferation through several signaling networks.[3,6,7]

In addition to this; fat cells may influence tumour growth regulator functions in other cells. For example mammalian target of rapamycin (mTOR).[3]

Leptin and adiponectin

Fat cells produce hormones called adipokines (such as leptin and adiponectin) that stimulate or inhibit cell growth. Leptin is thought to promote cell proliferation, and obesity is associated with elevated levels of leptin due to the larger adipose tissue volume. Adiponectin is thought to have anti-proliferation effects on cells and tends to be at lower levels in obese people.[6,7,10]

Alterations to inflammatory cytokines

Obesity causes formation of an expanded compartment of adipocytes and in turn, the accumulation and activation of immune cells. Signalling from these cells is associated with an increase in TNF-α (tumour necrosis factor-alpha) and IL-6 (Interleukin-6) activity. Increased levels of IL-6 can activate signalling to promote cell proliferation and survival. Increased TNF-α can inhibit negative regulator activity to further support a pro-growth state.[6,7,10]

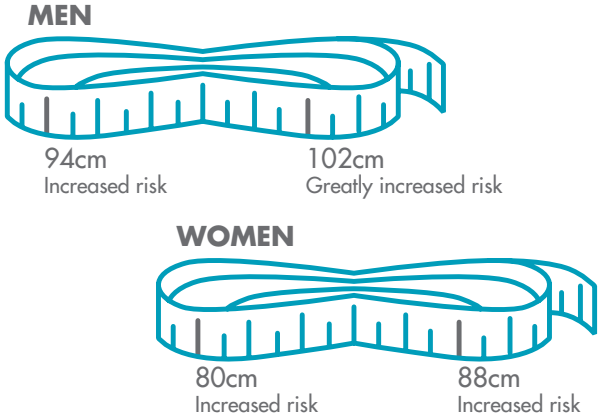
Measuring overweight and obesity

Overweight and obesity can be measured by the Body Mass Index (BMI).

CALCULATE YOUR **BMI** = WEIGHT [KILOGRAMS] / HEIGHT X HEIGHT [METRES]

Underweight	<18.5
Normal range	18.5–25
Overweight	25–30
Obese class I	30–35
Obese class II	35–40
Obese class III	>40

It is also important to consider waist circumference when considering risk factors, as a **higher waist circumference** has also been shown to increase risk for a variety of cancers.[11]



Strength of the evidence for a cancer-preventative effect of the absence of excess body fatness, according to cancer site or type

Cancer site or type	Strength of the evidence in humans	Relative risk of the highest BMI category evaluated versus normal BMI (95% CI)
Oesophagus: adenocarcinoma	Sufficient	4.8 (3.0–7.7)
Gastric cardia	Sufficient	1.8 (1.3–2.5)
Colon and rectum	Sufficient	1.3 (1.3–1.4)
Liver	Sufficient	1.8 (1.6–2.1)
Gallbladder	Sufficient	1.3 (1.2–1.4)
Pancreas	Sufficient	1.5 (1.2–1.8)
Breast (post-menopausal)	Sufficient	1.1 (1.1–1.2)
Corpus uteri	Sufficient	7.1 (6.3–8.1)
Ovary	Sufficient	1.1 (1.1–1.2)
Kidney: renal cell	Sufficient	1.8 (1.7–1.9)
Meningioma	Sufficient	1.5 (1.3–1.8)
Thyroid	Sufficient	1.1 (1.0–1.1)
Multiple myeloma	Sufficient	1.5 (1.2–2.0)

From the International Agency of Research into Cancer[2]

Key points for discussing obesity and cancer link with patients

Obesity and cancer link

- Being overweight or obese can **increase your risk of 13 types of cancer**.
- **Visceral fat** around our waist and organs is dangerous and can increase your risk of some cancers and other chronic diseases.
- **Excess body fat,** especially excess 'visceral fat' that sits in our middle around our organs doesn't just sit there and store energy. The fat is active and it produces chemicals and hormones which travel around our bodies.
- These changes can **alter how the cells in your body divide** and this may increase your risk of some cancers.

Healthy lifestyle recommendations to reduce cancer risk

One in three cancers may be preventable. Following the recommendations below can help reduce the risk of cancer, not just those associated with obesity. It is important to consider all preventative behaviours like screening for cancer, avoiding smoking, limiting/avoiding alcohol, avoiding exposure to UV radiation, choosing a healthy diet, getting adequate exercise and weight management.

Diet, exercise and weight advice for patients

- **If you are a healthy weight:** follow a healthy diet, exercise and avoid weight gain.
- **If you are overweight:** follow a healthy diet, exercise and try to lose some weight or avoid gaining more weight.
- Even if you are overweight and have difficulty losing weight **you can still decrease your risk of cancer** by improving your diet and exercising more.
- **Choose a diet** rich in vegetables, fruit, legumes and wholegrains.
- **Fast foods**, highly **processed foods** and foods high in added **sugar** should be **limited.**
- **Sugary drinks** contribute to weight gain and should be **limited** or avoided altogether.
- To reduce the risk of cancer, you should **limit your intake of alcohol** to match the national guidelines – drink no more than 2 standard drinks a day or, better still, avoid alcohol altogether.
- **Red meat** should be consumed in moderation (less than 500g cooked meat per week).
- Intake of **processed meats** should be limited.

For patients who have difficulty losing weight

It may be difficult for your patients to lose weight. It is important to recognise that even modest weight loss, or prevention of extra weight gain can help reduce their cancer risk.

It is also important to acknowledge other ways people can reduce their cancer risk, such as eating a healthier diet, doing more physical activity, avoiding smoking, limiting alcohol, participating in cancer screening and being SunSmart.

The link between sugar and cancer

- **Sugar is not a carcinogenic** (cancer-causing) substance but consuming too much sugar (particularly added sugars in processed beverages and foods) can contribute to obesity, which is an important risk factor for cancer.
- There is **no evidence** that consuming sugar makes cancer cells grow faster or causes cancer.
- Cutting out sugar will **not starve cancer cells**.
- All cells in your body prefer to use glucose/sugar for fuel. **Cancer cells** will also use **fat or protein for fuel** in the absence of sugar.
- It is **not recommended** to **cut out all** sugar or all carbohydrate foods.
- Cancer Council supports the **Australian Dietary Guidelines** that recommend people enjoy a wide variety of nutritious foods from the five food groups every day.
- It is also recommended that **adults and children limit intake of foods high in added sugars** such as confectionery, biscuits, cakes, sugar-sweetened soft drinks and cordials, fruit drinks, vitamin waters, energy and sports drinks.

Advice for patients with cancer

- Advise that messages to prevent cancer may not be appropriate for the treatment of cancer.
- Call the Cancer Council on **13 11 20** for information and support.
- Advise them to visit **cancerwa.asn.au**

Useful webpages

- LiveLighter
- Cancer Council WA
- National Dietary Guidelines
- National Physical Activity Guidelines

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