# MSCAN

# Website content: Cutaneous Squamous Cell Carcinoma (cSCC)

## Contents

# WHAT IS CUTANEOUS SQUAMOUS CELL CARCINOMA? (cSCC)

Cutaneous squamous cell carcinoma (cSCC) is a keratinocyte cancer, or a non-melanoma skin cancer. cSCC is the second most common skin cancer after basal cell carcinoma (BCC). Most keratinocyte cancers are not life-threatening.

It is estimated that about 580 of every 100,000 cSCC's are removed in Australia each year[1]. Although the number of cases is probably higher because unlike other cancers, keratinocyte cancers are not tracked by government databases.

## What are the different skin cancers?

The names of the cancers tell you where in the outer layer of the skin (the epidermis) the cancer has formed.

Basal cells: The basal cells form the bottom portion of the epidermis. These cells eventually move up, change, and become the squamous cells that flake off. If basal cells become cancerous, the condition is known as basal cell carcinoma (BCC).

Melanocytes: Melanocytes are the cells that produce a brown pigment called melanin to add colour to our skin. If these cells mutate and become cancerous, the condition is called melanoma.

Squamous cells: The squamous cells are found in the upper portions of the epidermis. These cells make a protein called keratin which is found in our skin, hair and nails. When the squamous cells grow out of control and become cancerous, they develop into squamous cell carcinoma.

**Different types of squamous cell cancers**

Squamous cells line areas on the inside and outside of the body. This means people can develop squamous cell cancers in areas away from the skin. Cancers can include squamous cell lung cancer, squamous cell head-and-neck cancer and squamous cell oesophageal cancer.

To avoid confusion, we add the word 'cutaneous' to the front of a cancer name to identify it as a skin cancer – cutaneous squamous cell carcinoma. Or you can say skin cancer for short.

## What does cutaneous squamous cell carcinoma look like?

Cutaneous squamous cell carcinoma (cSCC) can look differently in different people and in different locations.

- It occurs most commonly on sun-exposed skin, such as the back of the hands, ears, scalp, etc.
- It can occur in unexpected places like inside the mouth, on the genitals, inside the anus or beneath a fingernail or toenail
- It looks like red, scaly patches or scaly bumps
- It sometimes looks similar to a wart
- It grows over the course of weeks to months
- It is often painless but can be tender or painful
- It can crust over, be itchy and bleed
- It varies in size
- It can cause numbness, pain and muscle weakness if invading a nearby nerve
- When it is aggressive, it can invade blood vessels.

**References**

1. Pandeya N, Olsen CM, Whiteman DC. The incidence and multiplicity rates of keratinocyte cancers in Australia. Medical journal of Australia. 2017;207(8):339-343. doi:10.5694/mja17.00284

# What is Cutaneous Squamous Cell Carcinoma (cSCC) before it becomes cancer?

## Precancer spots or patches

**Actinic keratoses**

Actinic keratoses (ak-TIN-ik ker-uh-TOE-sees) are scaly spots or patches on the top layer of the skin. They are called precancers because they can turn into cutaneous squamous cell carcinoma (cSCC). That is why it is important to know what they look like.

Actinic keratoses are also known as solar keratoses and:

- are generally caused by sun damage.
- often look like small, dry, scaly or crusty skin patches.
- their colour varies from dark tan to white to flesh-coloured, or they are a combination of colours.
- they can be thick and have a rough texture that can feel like fine sandpaper.

It is hard to tell which actinic keratoses will develop into skin cancer, so your doctor will often remove them as a precaution.

## Early stages of cSCC

**Bowen's disease**

When an actinic keratosis develops into cSCC in the epidermis (the top layer of the skin), it is called Bowen's disease. Bowen's disease is also called squamous cell skin cancer in situ, intraepidermal carcinoma (IEC) or Stage 0 cSCC.

**How does it feel to touch?**

Bowen's disease or early stage cSCC can:

- Be a rough-feeling reddish patch
- Appear on the lip, often on the lower lip because of sun exposure
- Form a raised, round growth
- In rare cases, form a little horn, like you would find on an animal. The Bowen's disease horn has a bony core covered with keratin. These tumours can grow quickly and are a concern.

Bowen's disease is not an invasive cancer; however, treatment may be required as sometimes they develop into non-melanoma skin cancers.

## Know your spots

cSCC can present in many different ways, even on the same person. That is why it is important to become familiar with all the spots on your body. That way, you can notice new spots that are suspicious or changes in existing ones as part of an early-detection strategy. It is important to see a GP or dermatologist if you see anything suspicious.

# Risk factors for Cutaneous Squamous Cell Carcinoma (cSCC)

Skin cancer can strike anyone. In fact, 69% (more than two out of three) of Australians will develop at least one confirmed keratinocyte cancer in their lifetime[1].

The majority of skin cancers are caused by UV light exposure, however there are a range of different factors that could put you at risk for developing cutaneous squamous cell carcinoma (cSCC).

Risk factors for cSCC include:

- Cumulative, unprotected exposure to sunlight or other UV radiation. UV exposure during childhood and adolescence is a big risk factor, as is working outdoors and spending leisure time outside.
- Fair or light skin, although people with darker skin can also develop cSCC.
- Where you live. In Australia, the further north you live or spend time, the higher the rates of skin cancer[2]. Queensland has the highest incidence of keratinocyte cancers (including cSCC) in Australia[3].
- Men are more likely than women to develop cSCC[2].
- A history of previous skin cancers.
- A history of actinic keratoses, that is scaly spots on sun-damaged skin.
- Older age. The average age when people in Australia develop cSCC is 76[4].
- Infection with the human papilloma virus.
- Immunosuppression. Organ transplant patients, patients infected with the human immunodeficiency virus, and certain patients with blood cancer are examples of at-risk groups. In fact, depending on the type of organ transplant and the immunosuppression regimen, organ transplant recipients are 65-250 times more likely to develop cSCC than the general population.
- Certain genetic mutations. Such as albinism, when there is lack of colour in hair, skin or eyes; and xeroderma pigmentosum (XP), a condition in which the body cannot repair damage to DNA caused by the sun.
- Exposure to certain toxic chemicals such as arsenic, carcinogens in tar, pitch, soot, etc.
- Smoking and alcohol.

**References**


1. Olsen CM, Pandeya N, Green AC, Ragaini BS, Venn AJ, Whiteman DC. Keratinocyte cancer incidence in Australia: a review of population-based incidence trends and estimates of lifetime risk. Public Health Research & Practice. 2022;32(1). doi:10.17061/phrp3212203
2. Pandeya N, Olsen CM, Whiteman DC. The incidence and multiplicity rates of keratinocyte cancers in Australia. Medical journal of Australia. 2017;207(8):339-343. doi:10.5694/mja17.00284
3. Staples MP, Elwood M, Burton RC, Williams JL, Marks R, Giles GG. Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985. Medical Journal of Australia. 2006;184(1):6-10. doi:10.5694/j.1326-5377.2006.tb00086.
4. Cancer Council Australia, https://www.cancer.org.au/cancer-information/types-of-cancer/non-melanoma-skin-cancer

# HOW IS CUTANEOUS SQUAMOUS CALL CARCINOMA (cSCC) DIAGNOSED?

If your GP suspects you have a cutaneous squamous cell carcinoma (cSCC), you may be referred to a dermatologist.

Treatment for the cSCC may be completed in one appointment if the cancer is found very early.

**Process for diagnosing cSCC**

- Medical History: your GP or dermatologist will take a medical history. This will include asking about your sun-exposure history, any relevant medical information including medications you are taking, and a history of any skin cancers you have had and what your family has had.
- Full body skin check: A full head-to-toe skin examination (skin check) will be recommended to look for other problem areas. You can always ask your GP or dermatologist to perform a full body skin check if they don't suggest it, although you might need another appointment – you don't want to rush it.
- Consider a biopsy: the GP or dermatologist will determine if you need a skin biopsy. They will generally numb the skin and using a scalpel, will remove part or all of the spot from your skin. A biopsy is the only way to know whether the spot is cancer or not. The skin sample will be examined by a pathologist who will look at the tissue under the microscope.
- Extra tests: if your doctor is worried that the cancer has spread to the lymph nodes, they may request a lymph node test (a biopsy) as well as imaging studies of the lymph nodes (and potentially other areas).

**What is a biopsy?**
A biopsy is an important part of diagnosing what type of cancer you have. A biopsy is when the doctor or dermatologist uses a scalpel to remove part or all of the spot of concern from your skin or takes a sample from another part of your body. A specialist will look at that bit of skin under a microscope to determine if the spot is cancerous.

**What are lymph nodes?**
Lymph nodes are small lumps of tissue between 0.1cm and 2.5cm long. They are part of the body's immune system and help fight infection. Adults have hundreds of lymph nodes in their body. If the cancer spreads from the primary tumour, the cancer cells typically spread to the nearest lymph node before affecting other parts of the body.

# Preparing for a dermatology appointment for a suspected skin cancer

Your GP or dermatologist will review the biopsy procedure with you, discuss the potential risks and benefits, answer your questions, and obtain your consent before doing the biopsy. In most cases, a biopsy can be completed in one visit. It can leave a scar. Your doctor will provide you with specific details before the procedure.

## Pathology tests

After the biopsy is completed, the skin sample (specimen) will be sent to a pathology laboratory (lab) where it will be examined by a pathologist. A pathologist is a medical professional who uses laboratory tests and their expert knowledge of cells, tissues, and organs to diagnose disease.

The pathologist will examine the specimen with and without a microscope, measure its thickness, describe its location and appearance, and do special tests. Your diagnosis is based on the careful examination of the biopsied tissue.

## Pathology reports

The pathologist will write a pathology report. The pathology report is a detailed summary of your suspected skin cancer that helps determine your diagnosis and prognosis.

Pathology reports may look different from one lab to another, but they generally report the same details and measurements.

## What will the pathology report tell me?

The pathology report will contain some key information about the biopsy and the specimen, including:

- Whether the pathologist thinks it is cancer or not
- If there is cancer, what type
- The stage of the cancer based on the tumour characteristics
- Whether the cancer has any “high-risk/aggressive” features
- Depending on the biopsy type, there may be an indication of the depth of the invasion of the cancer.

## Some questions you could ask about your pathology report

Your GP or dermatologist will explain the pathology report and the results of your biopsy. If there is something that does not make sense, you can ask for it to be explained in a different way. Here are some questions that might be helpful.

- Is this a particular type of skin cancer?
- Can you draw me a picture to help me understand?
- Will I have more tests?
- Do I have any high-risk features? If so, how many and what are they?
- Is my skin cancer localised or has it spread to my lymph nodes—or beyond?
- Can I please have a copy of the pathology report?
- What is my prognosis (likely outcome of the cancer)? How did you establish that?
- What is the stage of my skin cancer?
- What are my treatment options?
- What are the potential risks / side effects?
- Do I need a referral to any other specialists (such as a medical oncologist, radiation oncologist, or head-and-neck surgeon)?
- Who can I contact if I have more questions?

*Image 1 health practitioner conducting routine skin check*

# HIGH-RISK FEATURES OF CUTANEUS SQUAMOUS CELL CARICNOMA (cSCC)

Certain features of a cutaneous squamous cell carcinoma (cSCC) can indicate whether the cancer is more likely to spread to other parts of the body. These high-risk features are related to the location, size and pathologic features of the tumour as well as certain characteristics of the patient.

When the pathologist examines the part of your skin that was taken by the biopsy, they will work out if your cancer is advanced or not.

If the tumour is localised, the pathologist will study the tumour for any high-risk features that mean it is aggressive.

**Primary tumour**
The primary tumour is where the cancer first develops in an organ or tissue. It can also be called the initial tumour or primary cancer. Cells from the primary tumour may break away and be carried to other parts of the body, where secondary cancers may form.

**Localised disease**
The part of your body around your primary cancer tumour is called the 'local' area. If your treatment team says something is 'localised', they are saying that all cancerous tissue remains near the area where the cancer first formed (the area near the primary cancer tumour).

**Aggressive**
Aggressive means that the cancer is more likely to spread to distant areas in your body or that it can act aggressively when they spread locally and invade other tissues such as your nerves, bone, and other structures. Tumours without high-risk features can be aggressive too.

**Advanced**
The word 'advanced' is used when the cancer has progressed beyond what can be removed by simple surgery or it has travelled to other parts of your body, perhaps reaching your bones or different organs. Advanced can also describe when you have had a number of treatments, but the cancer has come back (recurred) or is still there.

## High-Risk Features of the Primary Tumour cSCC

- **Large size**: any tumour that has a size greater than 20 mm (2 cm). 20mm is about the size of a $2 coin in Australia.
- **Problematic location**
  - On sensitive or mucosal locations such as the genitals
  - On areas that have lots of sun exposure, such as the central face (the mask area – see image), hands, and feet, particularly around the nails
  - On an area of your skin without hair
  - On a site with previous skin damage. This could include a site that is inflamed, has an active wound, has a scar, or has been treated with radiation before. This is called a Marjolin ulcer

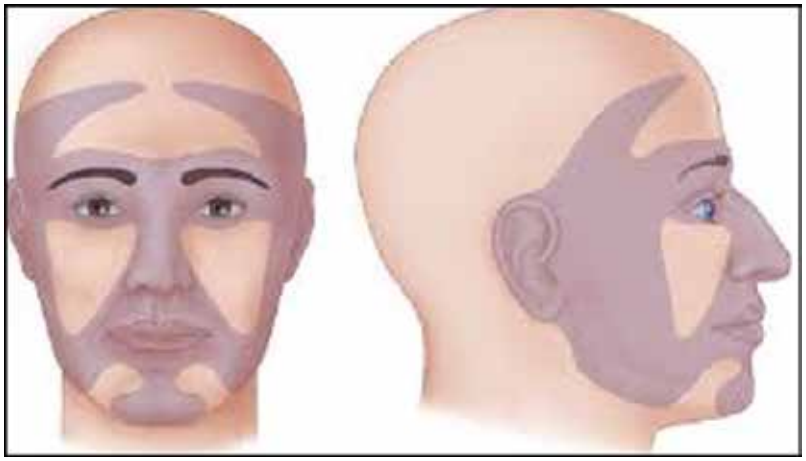


*Image 2: Tumours that arise in the "mask area" on the face are high risk (shaded in image)*

- **Specific Invasive Features**
  - Invading deeper than 6 mm below the skin surface, particularly deeper than fatty tissue
  - Invading bone, muscle, or cartilage
  - Growing into blood vessels or into nerves
- **Certain symptoms** causing pain and itchiness
- **Certain tumour subtypes** like acantholytic, desmoplastic, and metaplastic
- **Presence of multiple tumours**
- **A history of prior tumours coming back**
- **Less differentiation** - this detail about your tumour is something reported on your pathology report—it means the tumour is acting "younger" and less like a mature squamous cell carcinoma. This label or designation means it has greater potential to cause trouble.

## High-Risk Features of the Patient With cSCC

Patients who have experienced any of the following are at higher risk for aggressive forms of cutaneous squamous cell carcinoma (cSCC):

- Immunosuppression resulting from the immunosuppressive regimens used after organ transplantation and other medical conditions, infection with the human immunodeficiency virus (HIV), certain blood cancers or other immune modified disorders
- Continuing immunosuppressive medications for various medical disorders
- Older age with tumour(s) on the head and neck
- A history of very intense or prolonged sun exposure

# STAGING CUTANEOUS SQUAMOUS CELL CARCINOMA (cSCC)

The doctor will identify the stage of your cancer to help them create your treatment plan. The stage of a cancer describes how far the cancer has grown and spread in your body at the time of diagnosis.

Unfortunately, there is no internationally accepted staging system for squamous cell carcinoma. The Stages of Melanoma page provides general information about cancer staging. The factors in cancer staging are included in predicting the outcomes of squamous cell carcinoma, however there are more risk factors that need to be considered.

The different diagnoses (or stages) of cutaneous squamous cell carcinoma (cSCC) are detailed below from low to high risk, with some helpful images so you can see how the cancer changes. The following information reflects the common terminology used in Australia for cSCC.

## Local Cutaneous Squamous Cell Carcinoma – Low Risk

Local cutaneous squamous cell carcinoma (cSCC):

- is generally characterised by smaller tumours with shallow depth of invasion and sparing of local lymphatic or blood vessels and nerves
- tumours can be found anywhere on the skin
- has a very low likelihood of advancing locally, becoming metastatic, or recurring (coming back after treatment).

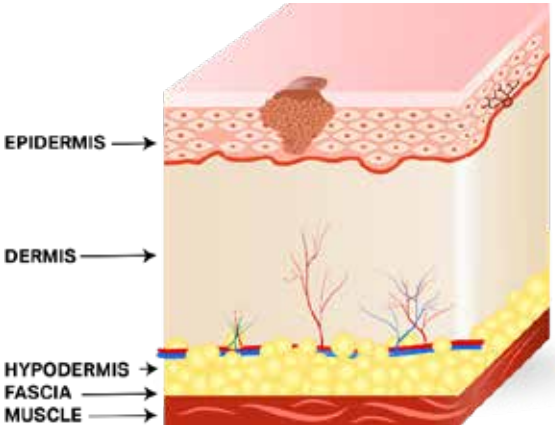



*Image 3: This image shows an in situ or Bowen's disease tumour, where the tumour has not penetrated past the epidermis*

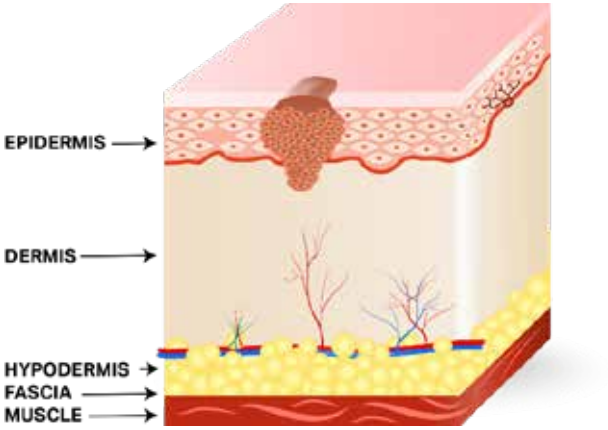



*Image 4: This image shows a low-risk squamous cell skin cancer that has penetrated a little further (into the dermis) than the in situ tumour.*

## Local Cutaneous Squamous Cell Carcinoma – High Risk

The tumours diagnosed under this category are still localised however they have some high-risk features including:

- tumours being larger and invading deeper into the skin and tissue
- potential to invade nearby nerves and blood and lymphatic vessels
- greater likelihood of becoming locally advanced, coming back after treatment (recurrence), or spreading (metastasis).

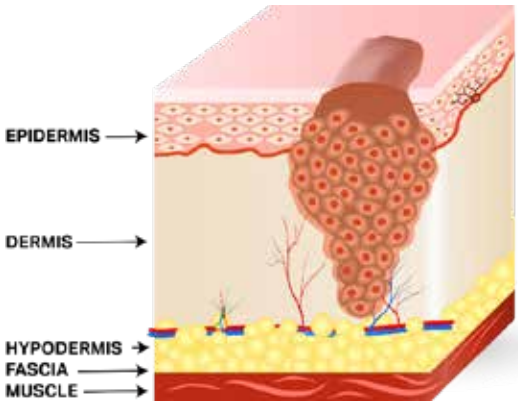



*Image 5: This tumour extends further down into the dermis and involves the blood vessels, which is a high-risk feature.*

**Recurrence**
Cancer that comes back after treatment.

**Metastasis**
Metastasis is when the cancer has spread to a different part of your body from where it started. If this happens, your treatment team might say the cancer has 'metastasised'.

**Lymph nodes**
Lymph nodes are small, seed-shaped structures that contain clusters of immune cells. Their function is to filter the lymphatic fluid, which helps to clear waste material from the tissues and deliver white blood cells to fight infections. Adults have hundreds of lymph nodes throughout the body, notably in the neck, armpit and groin.

# Advanced disease

Advanced disease includes tumours that have spread deep below the skin making surgery difficult and unlikely to succeed in at removing the entire tumour. Other advanced tumours may have advanced to the lymph nodes or to sites far away in the body.

## Locally Advanced Cutaneous Squamous Cell Carcinoma

Locally advanced cSCC are tumours that have already penetrated deep below the skin.
The tumour can be characterised as:

- being greater than or equal to 2 cm
- having invaded into blood or lymphatic vessels or nerves
- having invaded into the fascia (the connective tissue covering the muscle that is below the subcutaneous fat), or underlying muscle
- having invaded into bone, potentially causing minor erosion of the bone surface (cortex) or even breaking into the deeper parts of the bone including the bone marrow

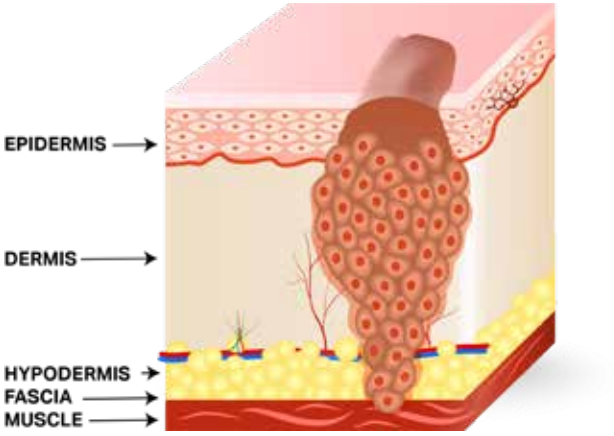


*Image 6: This tumour has invaded into the fascia (the connective tissue covering the muscle that is below the subcutaneous fat)*

# When cSCC spreads

Approximately 4% of cSCC will metastasise (spread) to the regional lymph nodes or to distant sites (other parts of the body).
Patients who are immunosuppressed may have a two- to three-fold higher risk of metastasis, which means the risk for metastasis can be as high as 12%.

## Regional Cutaneous Squamous Cell Carcinoma

Regional cSCC (or regional disease) is characterised by cancer that has spread to nearby lymph nodes. Cancer cells typically spread from the primary tumour to the nearest lymph node before traveling to other parts of the body. Regional disease is also called Nodal disease.

### How is regional disease diagnosed?

If the lymph node feels swollen or if lymph nodes are identified by imaging, then the doctor will take a sample from the lymph node for testing. There are two ways to test the lymph nodes:

- fine needle aspiration: a hollow thin needle is attached to a syringe to remove fluid and small amounts of tissue to examine.
- core needle biopsy: a larger needle with a larger hollow centre (bore) is used to remove a small section of tissue to give the doctor more information

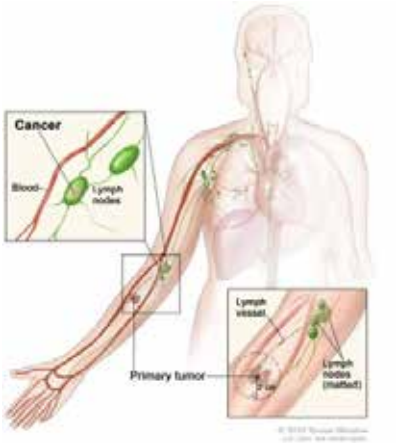


*Image 7: Cancer involving the lymph nodes. The diagram shows the primary tumour as well as the affected lymph nodes.*

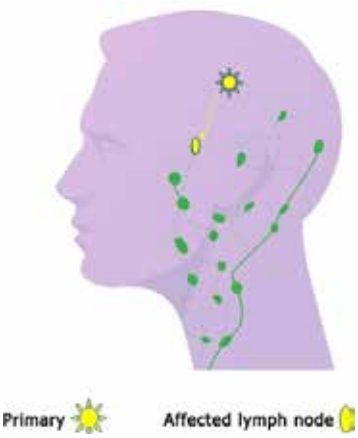


*Image 8: Skin cancer on the scalp that has spread through the lymphatics to a lymph node on the head*

## Distant Metastatic Cutaneous Squamous Cell Carcinoma

Distant metastatic cutaneous squamous cell carcinoma (cSCC) means the disease has spread to other site(s) in the body. The advanced cancer can reach far away lymph nodes or the lungs, brain or other organs.

Your doctor can advise you if you need imaging to look for metastatic disease. Imaging may be ordered if you have certain symptoms or abnormal laboratory tests. The additional imaging may include computed tomography (CT) or positron emission tomography - computed tomography (PET-CT), or MRI.

It is important to note that most patients with cSCC will not need a CT scan as the risk of distant metastatic disease is only 0.4%.

*Image 9: Yellow sunburst shows the site of the primary tumour on the neck and spread to the lung, liver, and bone*

**Types of scans**

Below are three types of scans – all three can be used to help diagnose disease (such as cancer), plan treatment, or find out how well treatment is working.

**CT Scan**

A computed tomography (CT) scan uses a computer linked to an x-ray machine to make a series of detailed pictures of areas inside the body. The pictures are taken from different angles to create three-dimensional (3D) views of tissues and organs. A dye may be injected into a vein or swallowed to help the tissues and organs show up more clearly on the pictures.
Also called CAT scan, computed tomography scan, computerised axial tomography scan, and computerised tomography.

**PET Scan**

A positron emission tomography (PET) scan provides pictures of how the body is working. A small amount of radioactive glucose solution is injected into the body to find cancerous areas. Cancerous areas show up brighter in the PET scan because they take up more of the glucose.

**PET-CT Scan**

PET-CT is a procedure that combines the pictures from a PET scan and a CT scan. The PET and CT scans are done at the same time with the same machine. The combined scans give more detailed pictures of areas inside the body than either scan gives by itself.
Also called positron emission tomography-computed tomography scan.

**MRI Scan**
Magnetic resonance imaging (MRI) is a scanning technique that uses magnets and radio waves to generate images of the organs in the body. MRI is helpful in getting images of soft tissues, including the brain, that may be affected by cancer. It does not use X-rays. Sometimes the test is used with contrast. Other times it is not. However, some people cannot receive MRI tests because of metals in their bodies or for other reasons. There is no radiation associated with an MRI test.

## Clinical consideration: do I need an MDT?

For 95% of cutaneous squamous cell carcinoma (cSCC) cases, your GP, dermatologist or surgeon can manage the disease surgically. But if your tumour has high-risk features, it might make sense to seek out a dermatologist who works in a multidisciplinary team (MDT) setting like a hospital.

An MDT can include experts in radiation oncology, surgical oncology, head-and-neck surgery, and medical oncology.

If your doctor cannot cure you surgically, an MDT approach might be needed to treat your cSCC. Typical situations that warrant this approach include:

- Surgically challenging (or high-risk) tumours in the head-and-neck region
- Progressive growth of the tumour
- Tumours arising in immunosuppressed patients
- Tumours arising in skin with chronic trauma or within an ulcer
- Disease that has spread to the regional lymph nodes
- Disease that has spread (metastasized) to bone, liver, lung, etc.
- Tumours that have recurred.

Talk to your doctor about what is the best treatment option for your diagnosis. Your doctor can recommend where you could go for further advice and refer you to specialists.

Note: Patients who are immunocompromised after solid organ transplantation have special considerations in terms of reducing their immunosuppression therapy and/or switching to a mammalian target of rapamycin (mTOR) inhibitor when they have a life-threatening skin cancer or rapid development of multiple tumours. In these settings, the transplant team should be consulted as part of the multidisciplinary cSCC management team.

# TREATMENT OPTIONS FOR CUTANEOUS SQUAMOUS CELL CARCINOMA(cSCC)

Your pathology report will identify the features of your cutaneous squamous cell carcinoma (cSCC). Your doctor will explain the results of the pathology report and help you understand the stage of cancer you have. Then it is time to plan your treatment strategy.

Remember, you can always ask your treatment team questions about your proposed treatment plan and to explain any words or terms that you are not familiar with.

## Surface or Destructive Therapy

These treatments are applied directly to your skin to treat cSCC.

### Curettage and Cautery (C&C)

Curettage and cautery involves the doctor scraping the cancer from your skin (curettage). Heat is applied to destroy any remaining cancer cells (cautery), which also stops any bleeding. The curettings will be sent to pathology for review, including looking for any high-risk features.

**Advantages:**

- It is quick and often completed in one visit
- It does not require stitches
- It allows rapid treatment of multiple cancers at the same time, for high-risk groups who have more than one cSCC.

**Disadvantages:**

- It does not work well on areas of the body that have hair
- It generally does not heal as well as an excision
- If the tumour is deeper than expected, the tumour may still need to be surgically removed
- It is not as effective as surgery
- It can be difficult for the pathologist to determine all the details of the tumour, particularly the depth of the tumour, given the small sample provided by the curettings.

### Cryotherapy

Cryotherapy involves applying a cold substance, such as liquid nitrogen, to the tumour and freezing off the tumour. Cryotherapy may be considered for low-risk cSCC when more effective therapies are not recommended or are impractical. It can also be considered for patients with conditions that cause their body to form large numbers of tumours.

## Surgery

Treatment for cSCC may involve surgery to remove some or all of the cancer tumour. Your treatment team will explain why they recommend surgery and what they hope the outcome will be. Some patients require several surgeries to remove all the cancer tumours that can be identified.

Some surgery can leave scarring on your body and can be disfiguring.

Some patients with advanced cSCC might require reconstructive surgery to repair the skin or other areas of the body where the cancer has caused damage. Reconstructive surgery can have both functional and cosmetic goals, so it is important to discuss and understand what the expected surgical outcome is with your surgeon.

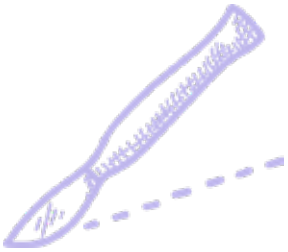
Benefits of surgery:

- Surgery is one of the best methods to control or cure a cancer.
- Important diagnostic tests can be done on the parts of the cancer tumour that has been removed.
- Surgery may help to relieve symptoms that you experience as a result of the cancer.
- While not commonly done, surgery can remove any remaining areas of cancer after drug therapy or radiation therapy has shrunk the primary cancer tumour.

There are two general types of surgery for cSCC:

## Wide Local Excision

A dermatologist (or specialised surgeon, often a plastic surgeon) cuts out the cancer and an area around the tumour called a wide margin. The wide margin removes extra skin around the tumour to ensure the doctor has removed all the cancer. If there is a big enough margin of normal skin around the cancer cells, your treatment is complete. If not, your doctor may need to go back and take more.



## Mohs Micrographic Surgery (MMS)

Mohs (rhymes with nose) surgery is recommended for cSCC that is likely to recur (come back) or is in an area where you don't want to remove a lot of skin. For example, around the face, neck, hand, fingers or toes.

In Mohs (also called microscopic controlled excision) surgery, you are usually awake while the doctor removes the smallest amount of tissue needed to treat the cancer.

The doctor removes the skin cancer that can be seen. Then a thin layer of surrounding skin is cut away and examined under a microscope. If cancer cells are found in that additional layer, the process will be repeated until no cancer cells can be seen. The doctor will then decide the best way to treat the wound.

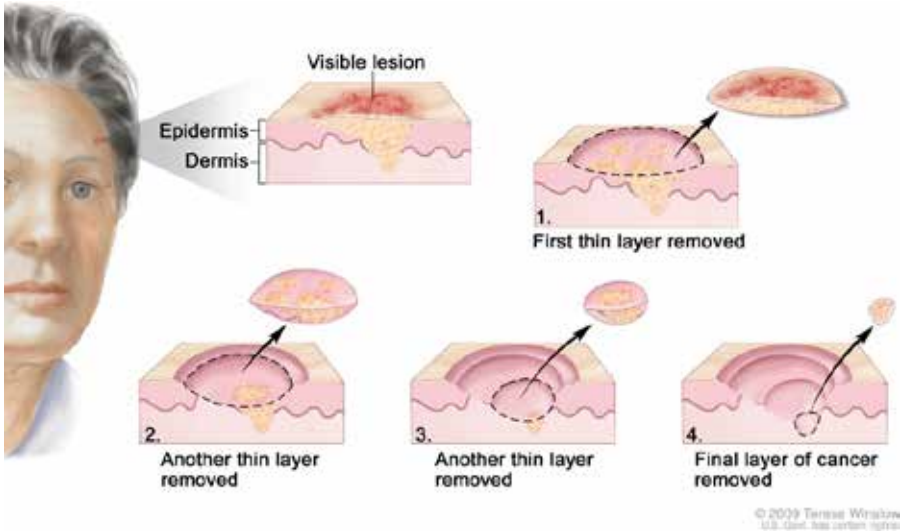



*Image 10: Mohs Micrographic Surgery (MMS)*

## Radiation Therapy or Radiotherapy

Radiation therapy uses high-energy particles to damage the DNA of cancer cells. The damage ultimately leads to the targeted cancer cells dying. The radiation injures both normal cells and cancer cells. However, normal cells can repair themselves while cancer cells can't and die after treatment.

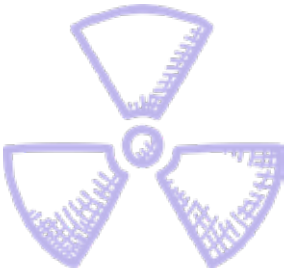
There are a number of reasons why your treatment team may suggest radiation therapy could be a good treatment option for you. Radiation therapy can:

- Be used after surgery to prevent the cancer from coming back - this is the most common use for radiation therapy.
- Be an alternative to surgery if you cannot have or do not wish to have surgery. Reasons why patients may not be able to have surgery can be because the surgery required is too dangerous or perhaps the patient's general health is not strong enough to tolerate surgery.
- Help protect organs, like the nose or ears, if they are located close to the tumour.
- Be used to control the burden of many skin cancers located over an area of the body. For example, on the scalp, forehead, nose, ear or limbs.
- Help reduce symptoms and aim to control the tumour from getting worse in situations where the cancer cannot be cured, such as in a palliative care setting.
- Be helpful in urgent situations where the tumour is causing significant bleeding, pain, obstruction or compression of other organs or the spinal cord.

Radiation therapy can cure cancer, but it is most effective in combination with surgery.

The different types of radiation therapy used to treat cSCC are:

- Superficial radiation therapy: Radiation beams are sent just beneath the skin, treating only the tumour
- External beam radiation therapy: High-energy beams of radiation are directed into the tumour in order to kill cancer cells, but no radioactive sources are placed inside your body
- Brachytherapy: Radioactive implants are placed directly inside (or near) the cancer. Also called internal radiation.



Photodynamic therapy, a treatment that uses light-activated radiotherapy, is not considered effective for cSCC. Laser therapy is also not considered effective for cSCC.

You can receive radiation therapy in a hospital or at a standalone treatment centre. Radiation therapy is usually provided as outpatient treatment which means patients generally do not need to be admitted to hospital.

Side effects of radiation therapy can include red, dry and sore skin around the area being treated. Remember to ask your treatment team about the possible side effects specific to your treatment so that you can be prepared.

**Radiation Therapy**

For more information about radiation therapy, check out this great website by the Faculty of Radiation Oncology of the Royal Australian and New Zealand College of Radiologists (RANZCR). It includes videos of patients explaining their experience as well as lots of helpful information.
https://www.targetingcancer.com.au/

**Key terms**
The word 'adjuvant' is used to identify treatment that helps the primary treatment. For cSCC, the primary treatment is usually surgery, and adjuvant treatment may include immunotherapy, targeted therapy, chemotherapy or radiation therapy.
Neoadjuvant Therapy – is cancer treatment given **before** the primary treatment to help reduce the size of the tumour or kill cancer cells that have spread.
Adjuvant Therapy – is additional cancer treatment given **after** the primary treatment aimed at killing any remaining undetectable cancer cells and lowering the risk that the cancer will come back.

**Curative**
Treatment given to damage or kill cancer cells.

## Systemic Therapy

Systemic Therapy is a treatment using substances that travel through the bloodstream to affect the whole body.

### Immunotherapy - Cemiplimab

Immunotherapy is a treatment that gives your immune system more power to fight your cancer. Immunotherapy can be used to treat adult patients with advanced cSCC when the cancer has spread beyond the primary tumour, or the cancer is locally advanced and cannot be cured with surgery or radiation therapy.

Every day, inside your body, your immune system recognises dangerous things — cancer cells, foreign invaders like bacteria and some viruses — and hunts them down and destroys them. However, some cancer cells can hide from your immune system. Other cancer cells can stop your immune system from doing its job by putting the brakes on it. The immune system may not realise these cells are cancer cells, which may explain why the cancer cells keep growing and multiplying.

Immunotherapy takes the brakes off the immune system, allowing it to identify and destroy cancer cells.

Immunotherapy for advanced cSCC, called cemiplimab (LIBTAYO®), has been approved for use in Australia. It can be prescribed for the treatment of adult patients with metastatic or locally advanced cSCC who are not candidates for curative surgery or curative radiation.

Cemiplimab is given in the vein (IV, intravenously) every three weeks in a hospital.

Cemiplimab belongs to a class of drugs called 'programmed cell death protein 1' (PD-1) inhibitors. PD-1 inhibitors reactivate part of the immune system (the T-cell system) that has been suppressed by cancer cells. When this T-cell system is reactivated, it can then do its job and seek out and kill cancer cells.

Immunotherapy may take some time to work. In the early stages of starting immunotherapy, your tumour site might look like it is getting worse. Talking to your treatment team can help monitor the progress of your treatment.

In clinical trials, cemiplimab shrank tumours in about half the patients with cSCC. This shrinking lasted six months or longer in 61% of the patients who responded to cemiplimab. A small proportion (about 4%) of patients had their tumours disappear completely. Cemiplimab can cause side effects such as lung problems, intestinal problems, liver problems, hormonal issues, kidney problems, and skin issues such as rash, blistering and sores in the mouth.

## Chemotherapy

Some patients with advanced cSCC may benefit from treatment with chemotherapy if other treatment options are not successful. Chemotherapy involves receiving medication through a needle into your vein, similar to immunotherapy. Chemotherapy is different to immunotherapy because the medication targets rapidly dividing cells, such as cancer cells, whereas immunotherapy boosts your immune system to identify and destroy the cancer cells.

Your treatment team will provide information about the chemotherapy if they think you would benefit from this treatment.

# TREATMENT OPTIONS BY STAGE OF CUTANEOUS SQUAMOUS CELL CARCINOMA

When selecting the treatment for your cutaneous squamous cell carcinoma (cSCC), you and your doctor will discuss the stage of your disease, any other medical conditions you may have and your personal preferences for different types of therapy.

This section reviews recommendations for treatment by the stage of the cancer and provides some guidance on how to weigh the efficacy, safety, convenience and other treatment factors that are important to you.

## Actinic Keratoses

Actinic keratoses are common pre-cancerous growths that may occasionally develop into cSCC if left untreated. Actinic keratoses are usually treated with cryotherapy or curettage and cautery, but they can also be treated with imiquimod cream, 5-fluorouracil cream, diclofenac gel or ingenol mebutate gel.

Separately or in addition, your doctor or dermatologist may recommend topical therapies (creams) you can apply at home. Examples include 5-fluorouracil (5-FU or Efudix) cream, diclofenac sodium gel, imiquimod (Aldara). Be sure to have a conversation about these options with your doctor or dermatologist to determine what treatments might be available the best approach for you.

These treatments act to destroy cancer cells and have side effects associated with them. This includes skin redness, localised pain or burning sensation, swelling, sores, ulceration, crusting, itching and tingling.

## Local Cutaneous Squamous Cell Carcinoma – Low Risk

For low-risk local cSCC, including Bowen's disease and cancer in situ, the standard treatment approaches are:

- Curettage and cautery (most commonly used for cSCC in situ)
- Local excision
- Radiation therapy (if surgery is not appropriate or feasible)
- Cryotherapy ablative laser (CO2 laser)

If surgery does not remove all of the cancer the first time, then further surgery can be done or your doctor might use one of the other options listed above.

## Local Cutaneous Squamous Cell Carcinoma – High Risk

If your cSCC tumour is high risk, then you may be a candidate for the following treatments:

- Wide local excision
- Mohs surgery
- Radiation therapy
- Systemic therapy (if curative radiotherapy is not feasible)
- A combination of the above.

If the surgery does not remove all the cancer the first time, another surgery may be an option. If that is not possible, radiation therapy, systemic therapy, a combination of therapies or a clinical trial may be considered. Also, if additional high-risk features are found, your doctor may alter the treatment plan.

## Locally Advanced Cutaneous Squamous Cell Carcinoma

If you have locally advanced cSCC, recommended treatment options include:

- Wide local excision
- Mohs surgery
- Radiation therapy
- Systemic therapy (if curative surgery or radiotherapy is not feasible)

## Regional Cutaneous Squamous Cell Carcinoma

Regional cSCC (or regional disease) is when the cancer has spread to nearby lymph nodes. If results from the fine needle aspiration or core biopsy identify lymph nodes that are cancerous, your treatment team will organise for you to have CT and PET-CT scans:

- A CT scan with contrast of the entire lymph node area to figure out size, number of nodes that have cancer
- A location PET-CT to rule out other metastases elsewhere in your body

Once scanning is complete, your doctors will determine if surgery is possible.

- If surgery is possible, the affected lymph nodes will be removed in a process called *lymph node dissection*. Radiotherapy is often used to kill any leftover cancer cells and prevent them from coming back (in this case, radiotherapy is a type of adjuvant therapy)
- If the surgery cannot be completed, your team may provide radiotherapy (if possible) and systemic therapy, most likely with cemiplimab.

## Distant Metastatic Cutaneous Squamous Cell Carcinoma

Systemic therapy or a clinical trial is recommended for the treatment of cSCC distant disease. Surgery or radiotherapy can be considered for symptomatic sites to ease symptoms (palliation).

**Lymph node dissection**
Lymph node dissection is a procedure to remove lymph nodes affected by cancer or lymph nodes in which there is a high chance that cancer has spread. Lymph node dissection is major surgery and there are potential short-term and long-term side effects.
Regional lymph node dissection: if only some of the lymph nodes are removed
Radical lymph node dissection: if most or all of the lymph nodes are removed

**Palliation**
Palliation means the relief of symptoms and suffering caused by cancer and other life-threatening diseases. Palliation helps a patient feel more comfortable and improves the quality of life but does not cure the disease.

# SIDE EFFECTS OF TREATMENT OF CUTANEOUS SQUAMOUS CELL CARCINOMA (cSCC)

All treatments can have side effects. It is important to know what side effects to expect from cutaneous squamous cell carcinoma (cSCC) therapies and how to work with your healthcare team to manage them.

## Surgery

Surgery carries both short- and long-term risks and can affect different body systems. It is important to keep your follow-up appointments with your surgery team and report any side effects immediately. Team members can offer strategies to address some of these complications.

### Nerve damage

Sensory nerve damage can occur with surgery, leading to localised numbness, a sensation of pins and needles, or burning or severe pain.

Motor nerve damage can occur with surgery, resulting in weakness or paralysis. In general, if the involved area is small, nerve damage may improve or resolve in approximately 12 months. However, sometimes the neurologic symptoms remain.

### Wound infection

Wound infection is an intermediate- to longer-term complication that can occur after surgery. The wound can break down or healing can be delayed.

### Lymphoedema

Lymphoedema (lim·fuh·de·muh) is an accumulation of lymph in the soft tissue (swelling) caused by the damage or removal of lymph nodes or lymphatic channels. It can occur either short term or long term for patients with cSCC who have had more extensive surgery.

A lymphoedema therapist can help with skin care, massage, bandaging, exercises, or a compression garment. This treatment is called complex decongestive therapy (CDT).

Disfigurement One of the biggest challenges with advanced cSCC is the potential for disfiguring cosmetic results. This can include loss or darkening of skin colour, suture marks, or scarring. Having a good reconstruction plan and follow-up with your surgeon is important.

## Effects of Radiation Therapy

Side effects of radiation are usually restricted to the area that has been radiated and can include:

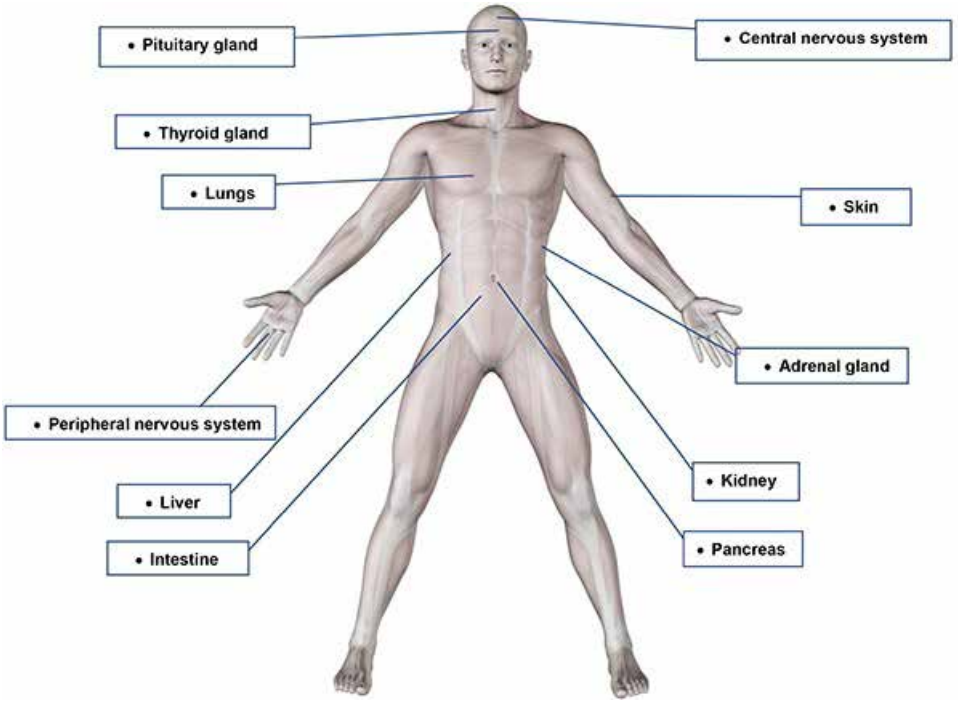
- Irritation of skin, ranging from redness to blistering and peeling
- Changes in skin colour
- Loss of hair in the area being treated
- Over time, radiation scarring may appear
- A long-term increase in new skin cancers in the area treated with radiation
- Damage to the salivary glands and teeth when treating cancers near the mouth
- Fatigue, taste changes, difficulty swallowing, and a less active thyroid gland (usually associated with radiation to the head and neck)
- In the long term, a loss of function of parts of the body.

It is important to talk with your radiology team about strategies to deal with these side effects. Some self-care approaches you can take include:

- Getting plenty of rest and establishing a good sleep routine
- Eating a balanced, nutrient-rich diet
- Taking care of the skin in the area that has received radiation. Be particularly careful to protect it from the sun, heat, and cold
- Avoiding irritating the skin by wearing tight or restrictive clothing
- Decrease stress and increase relaxation.

## Effects of Immunotherapy

Immune checkpoint inhibitors such as Libtayo®/ cemiplimab stimulate the immune system and can cause a range of side effects. These can be considered autoimmune in nature. The figure below shows the body systems that can be involved.




## Immunotherapy side effects

**Common side effects**: tiredness, rash, diarrhoea, muscle and bone pain.
**Concerning side effects**: lung, liver, skin, neurologic, cardiac and visual problems. Gastrointestinal inflammation and hormonal problems affecting glands like the adrenal, pituitary, thyroid glands, and the pancreas are also possible.

In immunotherapy clinical trials, serious side effects occurred in approximately one quarter or less of participating patients.

The management of the side effects of immunotherapy typically involves pausing or stopping immunotherapy and then managing the side effect. Reducing the dose of immunotherapy is generally not recommended. In cases with moderate side effects, corticosteroids are used, after which immunotherapy can be restarted. But in severe cases, the drug may need to be discontinued.