Melanoma and other skin cancers: a guide for medical practitioners

Australia has the highest rates of skin cancer in the world: 2 in 3 Australians will develop some form of skin cancer in their lifetime.

Skin cancer is divided into two main types

Melanoma

Melanoma develops in the melanocytic (pigment-producing) cells located in the epidermis. Untreated, melanoma has a high risk for metastasis.

The most common clinical subtype is superficial spreading melanoma (SSM), making up 55–60% of all melanoma. SSM is most commonly found on the head and neck (per unit area). Other common sites are the trunk in males and lower extremities in females. However, SSM can develop on any part of the body, including parts not heavily exposed to ultraviolet (UV) radiation.

In NSW:

- Melanoma is the third most common cancer diagnosed.
- Every year, there are around 5,000 new cases of melanoma and over 400 deaths from the disease.
- Men over 40, compared to women of a similar age, are more than 1.5 times more likely to be diagnosed with melanoma and 2.5 times more likely to die from it.
- People living in regional areas of NSW are more likely to be diagnosed and die from melanoma, compared to those living in major cities.

Keratinocyte cancer (previously called NMSC)

- **Squamous cell carcinoma (SCC)** develops from keratinocytes in the epidermis and is associated with risk of metastasis. Overall, SCC is most commonly found on the face, particularly the lip region, ears, nose, cheek and eyelid, and then on the neck, dorsa of hands and forearms. In males, SCC is commonly found on the head and neck, and in females, it is commonly found on the lower limbs, followed by the head and neck. Many SCCs arise from premalignant actinic keratoses.
- **Basal cell carcinoma (BCC)** also develops from keratinocytes in the epidermis and is the most frequently diagnosed cancer in Australians. In both sexes, BCC is most commonly found on the face (the eyelid, lip and nasolabial fold), followed by ears, nose and cheek. In males, BCC is common on the neck, back and shoulders. In females, BCC is common on the neck, shoulders and outer arms.

In 2021, there were over 1 million treatments for keratinocyte cancers in Australia.

Causes of melanoma and other skin cancers

- Unprotected exposure to UV radiation remains the single most important lifestyle risk factor for melanoma and other skin cancers.
- UVA and UVB radiation contribute to skin damage, premature ageing of the skin and skin cancer.
- Melanoma and BCC are associated with the amount and pattern of sun exposure, with an intermittent pattern carrying the highest risk. UV exposure in adulthood as well as in childhood contributes to BCC and melanoma risk.
- Premalignant actinic keratoses and SCC are associated with the total amount of sun exposure accumulated over a lifetime.
- Other risk factors for keratinocyte cancers can include exposure to some chemicals (e.g. arsenic); radiation therapy and psoralen (PUVA) treatment for psoriasis; immunosuppressive therapy; HPV infection; and some rare genetic conditions predisposing people to skin cancer.

Risk factors

- Over 50 naevi (moles)
- Multiple dysplastic naevi
- Personal or family history of skin cancer (melanoma and keratinocyte cancers)
- Increasing age
- Working outdoors
- High levels of intermittent sun exposure (e.g. during outdoor recreation or sunny holidays)
- Fair skin that burns easily, freckles and does not tan
- Having fair or red hair and blue or green eyes
- Immune suppression and/or transplant recipients.

Gender

Men are more likely to develop and die from melanoma than women. Mortality from melanoma rises for males from 40 years and increases with age. Men over the age of 40, compared to women of similar age, are more than one and a half times more likely to be diagnosed with melanoma and two and a half times as likely to die from it.

Aboriginal and Torres Strait Islander peoples and other non-Caucasians

The incidence of melanoma in Aboriginal and Torres Strait Islander peoples is low. For the period 2011–2015, 25 Indigenous Australians died from melanoma - an average of 5 deaths per year.

The incidence of melanoma in non-Caucasians is also low. However, non-Caucasians are more likely to experience delayed diagnosis and have poorer clinical prognosis compared to Caucasians.

Non-Caucasians tend to develop clinical melanoma subtypes rare in Caucasian populations:

- Acral lentiginous melanoma on the palms of the hands and soles of the feet
- Subungual melanoma within the nail matrix.

Melanoma diagnosis

Superficial spreading melanoma (SSM)

Melanoma can develop in pre-existing moles in the skin or, more commonly, de novo.

- SSM is the most common form of melanoma.
- SSM can appear as a new spot, or an existing spot, freckle or mole that changes size, colour or shape.
- A patient diagnosed with SSM is at increased risk of new primary melanomas (relative risks ranging above 10).

(See examples on last page)

Nodular melanoma (NM)

This is a highly dangerous form of melanoma that grows and can metastasise quickly, and differs from SSM in appearance.

- NM has little radial growth within the epidermis but penetrates vertically into the dermis early.
- NM can develop de novo in normal-appearing skin, or within another type of melanoma.
- NM is more likely to be symmetrical and uniform in colour (red, pink, brown or black), is more frequently lighter coloured than SSM, and feels firm to the touch.
- Over time, NM may develop a crusty surface that bleeds easily.
- NM develops most commonly on the head and neck, in sun-damaged skin and in older people, particularly men.
- Approximately 10–15% of total melanomas diagnosed are NM.

(See examples on last page)

The ABCD(E) acronym can help distinguish an SSM from a normal mole:

A **Asymmetry:** the lesion is irregular in shape or pattern.

B **Border:** the border or outline of a melanoma is usually irregular.

C **Colour:** there is variation in colour within the lesion.

D **Diameter:** the lesion is usually greater than 6mm across. However, suspect lesions of smaller diameter should also be investigated.

E **Evolving:** the lesion changes over time (size, shape, surface, colour, symptoms e.g. itch).

The ABCD(E) acronym cannot be used to aid diagnosis of NM but the following features – EFG – can be of help:

E **Elevated:** the lesion can appear as a small, round and raised lump on the skin. Colour may be uniform throughout the lesion and may be black, brown, pink or red.

F **Firm:** the lesion feels firm to the touch.

G **Grows:** a nodule that has been growing progressively for more than a month should be assessed as a matter of urgency.

Lentigo Maligna (LM)

A slow growing form of melanoma in situ that can be difficult to recognise. LM can resemble a freckle and develops in heavily sun-damaged older skin, especially on the head and neck. Margin determination can be challenging and there is more frequent local recurrence than other types of melanoma. Incidence of LM is increasing.

Diagnosis tools

- Dermoscopy uses a hand-held magnifying device combined with either the application of a liquid between the transparent plate of the device and the skin, or the use of cross-polarised light. It allows the visualisation of diagnostic features of skin lesions that are not seen with the naked eye.
- **Dermoscopy increases diagnostic accuracy, confidence in diagnosis and reduces unnecessary excision of benign lesions. Training and utilisation of dermoscopy is recommended for clinicians routinely examining pigmented skin lesions.**
- Sequential digital dermoscopy imaging (SDDI) involves the assessment of successive dermoscopic images to allow the detection of suspicious dermoscopic change in melanomas that lack dermoscopic evidence of melanoma at a particular time.
- Total body photography allows the detection of suspicious change and is useful in high-risk patients or patients with dysplastic nevi syndrome.
- In vivo confocal microscopy allows non-invasive "optical biopsy" with the visualisation of the morphology and organisation of the cells in depth of the skin. It is useful for difficult diagnoses and margins (i.e. amelanotic melanoma, LM) in specialised centres.

Biopsy and excision for melanoma or suspicious naevi

- Excision of the entire lesion with a 2mm margin is recommended.
- Partial biopsies (punch biopsy or shave excision) are less accurate than excisional biopsy and should be avoided. If complete excision is impractical, a large incisional biopsy incorporating as much of the atypical part of the lesion as possible is the best alternative.
- The excision or biopsy should not interfere with subsequent treatment. For this reason, wide excisions, flap reconstructions, and curettage of suspicious lesions are contraindicated.

Any lesion that displays the EFG features over a period of more than one month should be investigated.

If melanoma is suspected, diagnosis should not be delayed and urgent referral or immediate excision with a 2mm margin is recommended.

Treatment for melanoma

Selecting appropriate primary treatment will depend on the Breslow thickness (vertical depth) of the tumour as measured and reported by tissue pathologists. Breslow thickness is used in the Tumour, Node, Metastases (TNM) staging system for melanoma tumours and is measured using the following system:

(pTis) Melanoma in situ.	The melanoma cells are found only in the non-vascular epidermis and have not penetrated into deeper tissue that contains blood vessels.
(pT1) Melanoma cells reach the upper part of the dermis.	The melanoma is less than 1mm thick.
(pT2) Melanoma cells reach the upper part of the dermis.	The melanoma is between 1mm and 2mm thick.
(pT3) Melanoma cells reach deeper into the dermis.	The melanoma is between 2mm and 4mm thick.
(pT4)	The melanoma is more than 4mm thick.

Treatment is based on the 5 stages (0 to 4) of tumour thickness (TNM classification) and involves the surgical removal of the melanoma. The recommended margins of excision are based on the Tis-T4 classification as follows:

(pTis) Melanoma in situ	5mm to 10mm clearance
(pT1) Melanoma <1.0mm	1cm clearance
(pT2) Melanoma 1.01–2.00mm	1–2cm clearance
(pT3) Melanoma 2.01–4.00mm	1–2cm clearance
(pT4) Melanoma >4.0mm	2cm clearance

NOTE: Evidence for optimal excision clearance for melanoma 2–4mm thick is unclear. The *Clinical Practice Guidelines* recommend it may be desirable to take a wider margin (2cm) for these tumours, depending on tumour site and surgeon/patient preference.

- **The T1-T4 (Primary Tumour Thickness):** classification is further divided into groups depending on presence of ulceration (a or b).
- **N classification (Regional Lymph Nodes):** is divided into a, b, and c for presence of cancer cells in the lymph nodes.
- **M classification (Distant Metastasis):** ranges from no evidence of distant metastasis (MX) to all visceral/any distant metastasis (M1c).

Other treatment options

Patients with melanomas >1mm thick should be referred to a specialised melanoma unit for multidisciplinary team input.

Surgery

- Sentinel lymph node biopsy (SLNB) may be considered for patients with pT2 (and higher risk pT1- i.e. pT1b) and thicker lesions and performed by trained practitioners in a specialised setting only.
- SLNB may also be offered to patients with >0.75mm thick with other high risk pathological features. Surgical resection of isolated metastases can be performed in both definitive and palliative treatment settings.

Radiation

- Radiation treatment can be used to treat LM when surgical approaches are considered less suitable. Post-operative radiotherapy can be performed for melanomas likely to recur locally or regionally. Radiotherapy can be used for palliative management of cerebral and bone metastases, and for other metastases where temporary local control is needed.

Oncology treatments

Systemic treatment is now recommended for patients with metastatic or inoperable melanoma, and for many patients with melanoma that has spread to lymph nodes after surgery. Survival in patients with melanoma has improved significantly since the introduction of the following agents:

- **Targeted therapy:** Inhibits the mitogen activated protein kinase pathway (BRAF and MEK inhibitor) in V600 BRAF mutant melanoma. These therapies are now used mostly in combination in order to achieve greater efficacy and reduced side effects. There are three combinations currently available.
- **Immunological therapy:** Modulates host/tumour immune responses via inhibitors of immune checkpoints on T cells, (namely the cytotoxic T lymphocyte associated protein 4 (CTLA-4) receptor and the programmed Death 1 (PD-1) receptor). The combination of immunological therapies seems more efficient but more toxic (including significant autoimmune toxicities). Current immunotherapy drugs in use include Nivolumab, Ipilimumab, and Pembrolizumab. The first two may be used in combination therapy whilst Pembrolizumab is used as a monotherapy.

NOTE: This field of treatment is changing rapidly with multiple new drugs and multiple new combinations. Benefits and harms of all treatment options require detailed discussion with the relevant specialist/s.

Follow-up for melanoma

Due to the risk of tumour recurrence and new primary melanomas, all patients require routine follow-up, the frequency of which will depend on the stage (0-4) of the primary tumour at time of diagnosis*:

- **Stage I:** follow-up annually for 10 years
- **Stage IIA:** every 6 months for 2 years, then annually for 8 years
- **Stage IIB and IIC:** every 3 to 4 months for 2 years, every 6 months during year 3, then annually for 5 years.
- **Stage IIIA-C:** every 3 months for 2 years, every 6 months during year 3, then annually for 5 years.
- **Positive SLNB** patients who have not tolerated adjuvant treatment or who have not had adjuvant treatment: 3-4 monthly ultrasound scans for a minimum of three years.

In Australia, up to 75% of patients detect their own recurring melanomas. Patients should be educated on recognising changes in their skin, have a professional full skin examination as deemed appropriate, and have further testing as required.

Information on self-checks for skin cancer is available at: www.cancercouncil.com.au/cancer-prevention/screening/checking-for-skin-cancer

** Clinical Practice Guidelines for the diagnosis and management of melanoma* can be found at: www.cancer.org.au

Keratinocyte cancer

Diagnosis

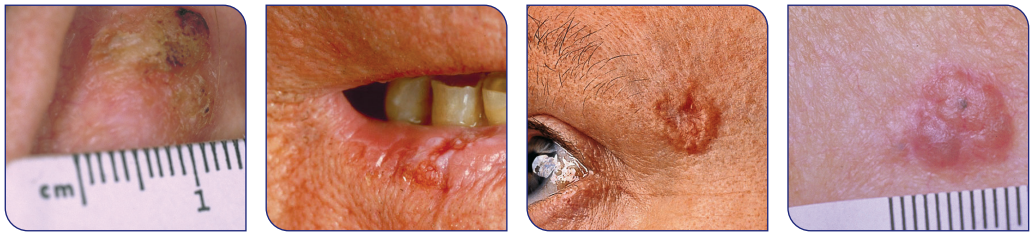
Squamous cell carcinoma (SCC)

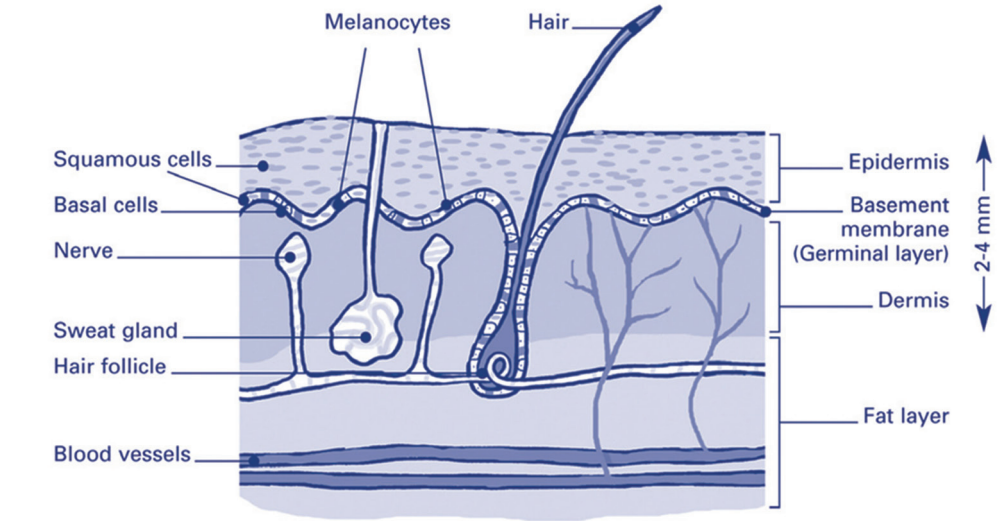
- SCC can spread to other parts of the body if not treated. Lesions on the face and scalp, histologically aggressive and/or larger tumours, and tumours arising in immune-suppressed individuals have a higher risk of metastasis.
- SCC appears as a thickened, red, scaly nodule that may bleed and ulcerate over time.
- SCC grows over a period of weeks to months.
- *(See more examples on last page)*

Basal cell carcinoma (BCC)

- BCC is the most common and least dangerous form of skin cancer.
- BCC appears as a well-defined lump or scaly area that is red or pearly in colour.
- BCC may bleed or become ulcerated early on, then heal and break down again.
- BCC usually grows relatively slowly.
- High-risk BCC subtypes (e.g. micronodular, infiltrating or morphoeic) and BCCs in immune suppressed individuals tend to have higher rates of recurrence after treatment.

(See more examples on last page)





Treatment

Treatment options for keratinocyte cancers include:

- surgical excision of the tumour and surrounding tissue
- radiotherapy
- curettage
- diathermy/electrodessication.

For biopsy-proven superficial lesions:

- cryotherapy
- application of topical agents (imiquimod cream, 5-fluorouracil cream, photodynamic therapy).

In general, the choice of treatment will depend on:

- tumour size
- thickness and grade
- aetiology
- histological features
- anatomic site
- patient preference and medical comorbidities.

Follow-up

Frequency of follow-up of patients treated for keratinocyte cancers for evidence of recurrence, metastasis and/or any new primary skin cancers will depend on histological clearance and risk level of the tumour, and on number of previous skin cancers.

Patients with multiple previous skin cancers should be followed up more regularly (three to six monthly) and educated on recognising changes in their skin (including, for patients with SCC, examination of draining lymph nodes).

Screening for melanoma and keratinocyte cancers

There is no evidence demonstrating that population-based screening for melanoma and keratinocyte cancers is effective in reducing morbidity or mortality, and it is not recommended.

Skin surveillance is recommended for patients identified to be at high risk of melanoma and keratinocyte cancers, including patients with a previous diagnosis of melanoma.

Skin self-examination (SSE)

Approximately 50% of melanomas are detected by the patient. There is no specific SSE technique or recommended frequency of self-examination that has been shown to reduce morbidity, however, regular skin examination may increase the probability of detecting skin cancer at an early and treatable stage.

Patients at high risk for melanoma should:

- be taught to self-screen (including examination of draining lymph nodes) and recognise suspicious lesions
- have a full body examination with a clinician every 6 months, supported by total body photography and dermoscopy.

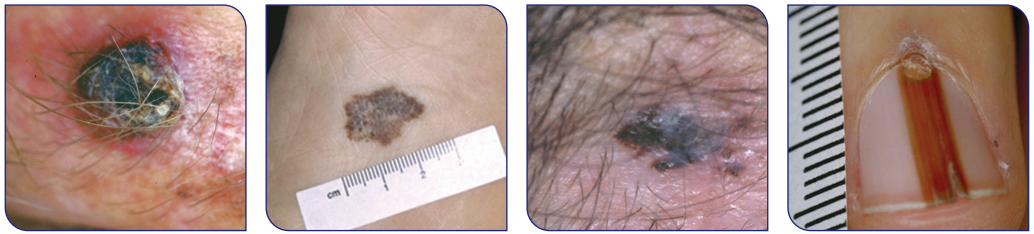
Patients treated for keratinocyte cancers should:

- be taught to self-screen and recognise changes to their skin
- have a full body examination with a clinician every 12 months or more frequently for patients at highest risk.

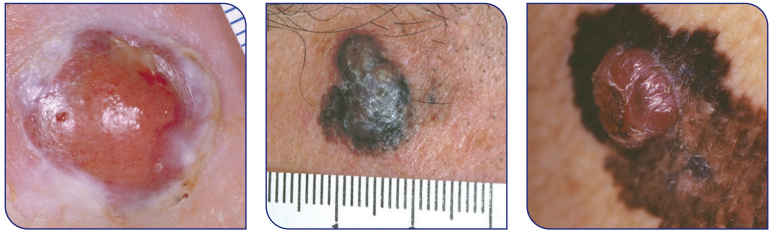
For the general population, the Australasian College of Dermatologists recommends that people examine their skin 4 times a year or as often as recommended by their medical practitioner.

Image references

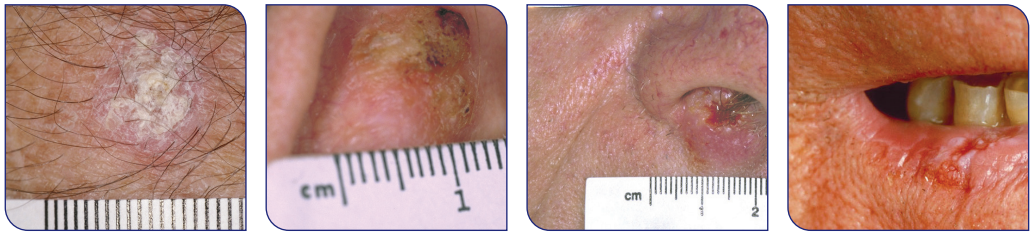
Superficial spreading melanoma (SSM)



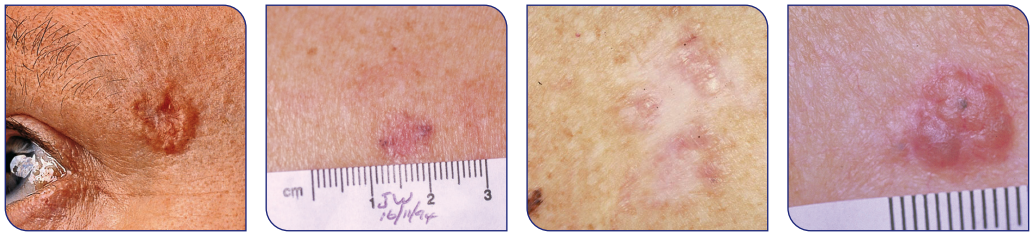
Nodular melanoma (NM)



Squamous cell carcinoma (SCC)



Basal cell carcinoma (BCC)



Images are supplied courtesy of the Sydney Melanoma Diagnostic Centre.

Key references

- Cancer Council Australia Melanoma Guidelines Working Party. *Clinical practice guidelines for the Diagnosis and Management of Melanoma (Features of melanoma, Biopsy, Sentinel Node Biopsy, Excision Margins)*. Sydney: Cancer Council Australia.
- Cancer Council Australia Keratinocyte Cancers Guideline Working Party. *Clinical practice guidelines for keratinocyte cancer*. Sydney: Cancer Council Australia.
- Cancer Institute NSW. Cancer in NSW. Melanoma Statistics.
- Australian Institute of Health and Welfare. Cancer in Aboriginal & Torres Strait Islander people of Australia. Canberra: AIHW; 2018.
- The Royal Australian College of General Practitioners. Guidelines for preventive activities in general practice. 9th edn. East Melbourne, Vic: RACGP, 2016.

Specialised melanoma and non-melanoma diagnosis and treatment services

- The Australasian College of Dermatologists website provides a "Find a Dermatologist" search function to assist in finding dermatologists by location dermcoll.edu.au
- Sydney Melanoma Diagnostic Centre
  Diagnosis and management of melanoma and pigmented lesions

  Sydney Cancer Centre
  2nd Floor, Gloucester House
  Royal Prince Alfred Hospital
  Camperdown NSW 2050
  Phone: 9515 8537
  Email: info@melanoma.net.au
- Melanoma Institute Australia
  Diagnosis, surgical management and medical treatment of melanoma

  The Poche Centre
  40 Rocklands Road
  Wollstonecraft NSW 2065
  Phone: 9911 7200
  Email: info@melanoma.org.au
- Calvary Mater Newcastle
  Diagnosis, surgical management and medical treatment of melanoma

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  Melanoma Unit located on Platt St
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  Email: melanoma@calvarymater.org.au
- The Skin Hospital
  Diagnosis and surgical management of melanoma and NMSC

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