

Melanoma and other skin cancers: a guide for medical practitioners

Australia has among the highest rates of skin cancer in the world: 2 in 3 Australians will develop some form of skin cancer before the age of 70 years.

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). 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 4th most common cancer diagnosed. Every year, more than 3,500 new cases are diagnosed and there are almost 500 deaths from the disease.
- The risk of developing melanoma increases with age. However, melanoma is the most common cancer in males aged 25–54 years and in females aged 15–29 years. It is the second most common cancer in females aged 30–54 years.
- The lifetime risk of developing melanoma by age 75 years is 1 in 24 for males and 1 in 34 for females.

Non-melanocytic skin cancer (NMSC)

- **Squamous cell carcinoma (SCC)** develops from the keratinocytes in the epidermis and is associated with risk of metastasis. 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 both sexes. In males, SCC is commonly found on the head and neck, and in females, it is commonly found on the upper limbs, followed by the head and neck. It is believed that 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. BCC is most commonly found on the face: the eyelid, lip and nasolabial fold, followed by ears, nose and cheek in both sexes. In males, BCC is common on the neck, back and shoulders, and in females, on the neck, shoulders and outer arms.

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.
- Premalignant actinic keratosis and SCC are associated with the total amount of sun exposure accumulated over a lifetime.
- Other risk factors for NMSC can include exposure to some chemicals (eg arsenic), radiation therapy, UVA and psoralen (PUVA) treatment for psoriasis, immunosuppressive therapy and some rare genetic conditions predisposing to skin cancer.

Risk factors for melanoma

- Multiple naevi
- Multiple dysplastic naevi
- Personal or family history of melanoma
- Increasing age
- High levels of intermittent sun exposure (ie during outdoor recreation or sunny holidays)
- Personal history of NMSC
- 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

In NSW, males are more than 1½ times more likely to be diagnosed with melanoma and almost 3 times more likely to die from it than females (after allowing for differences in age).

Mortality from melanoma rises steeply for males from 50 years and increases with age. The death rate for males aged:

- 50–54 years is twice that of females
- 55–59 years is 3 times that of females
- 75–79 years is 4½ times that of females.

Melanoma in non-Caucasian patients

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

Non-Caucasians are more likely to develop clinical melanoma subtypes rare in Caucasian populations:

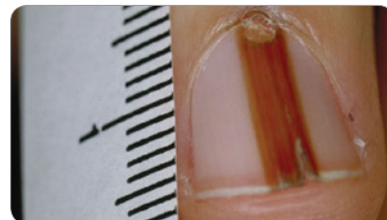
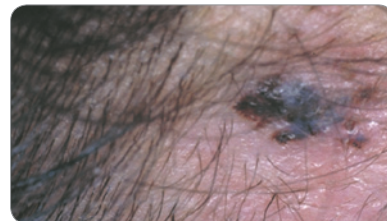
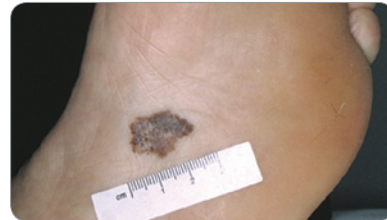
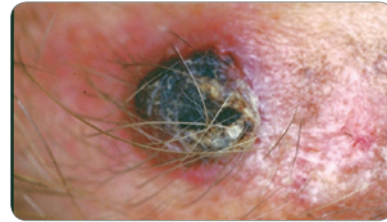
- Acral lentiginous melanoma on the palms of the hands and soles of the feet
- Subungual melanoma within the nail matrix.

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 melanoma is at increased risk of new primary melanomas (relative risks ranging above 10).



The ABCDE acronym can help distinguish a superficial spreading melanoma from a normal mole:

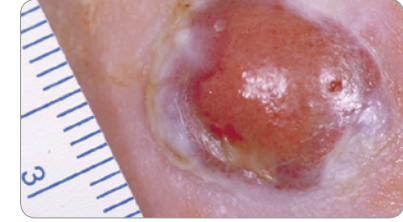
- A Asymmetry:** the lesion is irregular in shape or pattern.
- B Border:** the border or outline of a melanoma is usually irregular.
- C Colour:** there is variation in colour within the lesion.
- D Diameter:** the lesion is usually greater than 6 mm across. However, suspect lesions of smaller diameter should also be investigated.
- E Evolving:** the lesion changes over time (size, shape, surface, colour, symptoms eg itch).

If nodular melanoma is suspected, diagnosis should not be delayed, and urgent referral to a dermatologist or immediate excision is recommended.

Nodular melanoma (NM)

This is a highly dangerous form of melanoma that grows quickly. NM differs from SSM in appearance. NM has little radial growth within the epidermis but penetrates vertically into the dermis early. It 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, it may develop a crusty surface that bleeds easily.

- NM can become life threatening in 6–8 weeks.
- Approximately 15% of total melanomas diagnosed are NM.
- NM does not necessarily arise from a pre-existing mole and is commonly found on the head and neck.
- NM develops most commonly in older people, particularly men.



The ABCDE acronym cannot be used to aid diagnosis of nodular melanoma; however, the following features 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.

Biopsy and excision for melanoma or suspicious naevi

- Complete excision biopsy with a 2 mm margin is recommended.
- Partial biopsies (ie punch biopsies and shave excisions) can be less accurate than excisional biopsy and should be performed by trained practitioners.
- If a thick SSM or NM is suspected, refer patient to a dermatologist, surgeon with an interest in melanoma or a multidisciplinary melanoma unit as a matter of urgency.

Treatment for melanoma

Selecting appropriate primary treatment will depend on the Breslow thickness (vertical depth) of the tumour. Breslow thickness is measured using the following system:

- (pTis) Melanoma *in situ*. The abnormal 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 1 mm thick.
- (pT2) Melanoma cells reach the upper part of the dermis. The melanoma is between 1 mm and 2 mm thick.
- (pT3) Melanoma cells reach deeper into the dermis. The melanoma is between 2 mm and 4 mm thick.
- (pT4) Melanoma is more than 4 mm thick or it has invaded through the dermis and into the underlying fat.

Treatment is based on the T1–T4 classification. The surgical removal of the tumour with recommended margins of excision for each of the T-classification groups are:

- (pTis) Melanoma *in situ*: 5 mm clearance
- (pT1) Melanoma <1.0 mm: 1 cm clearance
- (pT2) Melanoma 1.0–2.0 mm: 1–2 cm clearance
- (pT3) Melanoma 2.0–4.0 mm: 1–2 cm clearance
- (pT4) Melanoma >4.0 mm: 2 cm clearance.

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

Other treatments options

Surgery

Sentinel lymph node biopsy (SLNB) should be discussed with patients with pT2 (and higher risk pT1 – ie pT1b) and thicker lesions, and performed by trained practitioners. Surgical resection of isolated metastases can be performed in both definitive and palliative treatment settings.

Radiation

Radiation treatment can be used to treat lentigo maligna 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.

Chemotherapy

- Chemotherapy may be offered for treatment of metastatic disease. Commonly used agents include dacarbazine (DTIC), fotemustine and carboplatin. Temozolomide is also occasionally used.
- Experimental agents, either alone or in combination with standard chemotherapeutic agents, may be offered as treatment of metastatic disease, within the context of clinical trials. Recently, new agents (eg BRAF inhibitors) have shown an improved response compared to previously low-efficacious chemotherapy agents.

Immunological therapies

- Interferon may be offered following surgical removal of melanoma that has not progressed past lymph nodes.
- Vaccines remain experimental, but may be offered within the context of clinical trials, either after surgical removal of early stage melanoma, or for low-volume metastatic disease.

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 of the primary tumour at time of diagnosis:

- 6-monthly intervals for 5 years then yearly for patients with stage I disease
- 3-monthly or 4-monthly intervals for 5 years then yearly (with ultrasound examination of regional nodes) for patients with stage II and III disease.

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.

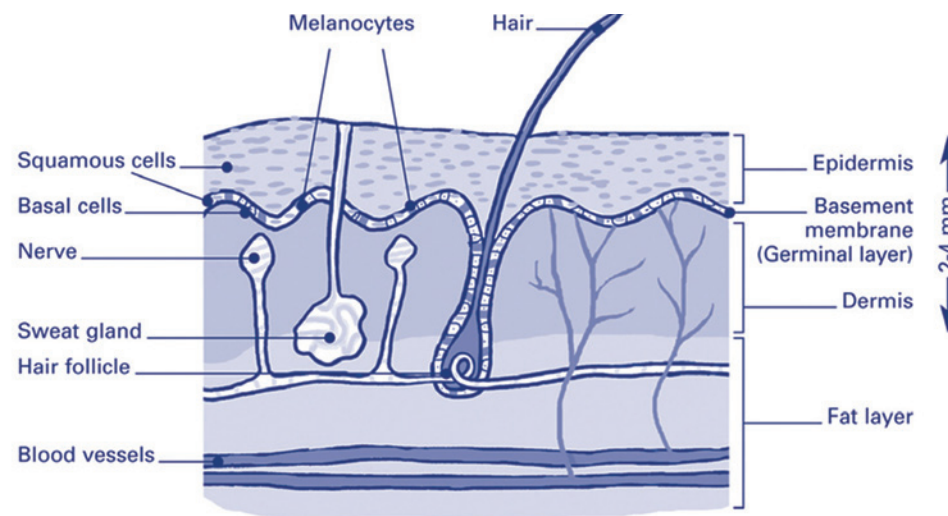
Survival

In Australia, for the period 2006-2010, the 5 year survival for melanoma was 94% for females compared with 89% for males.*

In NSW, the 5-year survival for melanoma is:

- 96% if detected when localised
- 63% if there has been regional spread
- 43% if there has been metastatic spread.

Clinical Practice Guidelines for the Management of Melanoma in Australia and New Zealand. www.nhmrc.gov.au



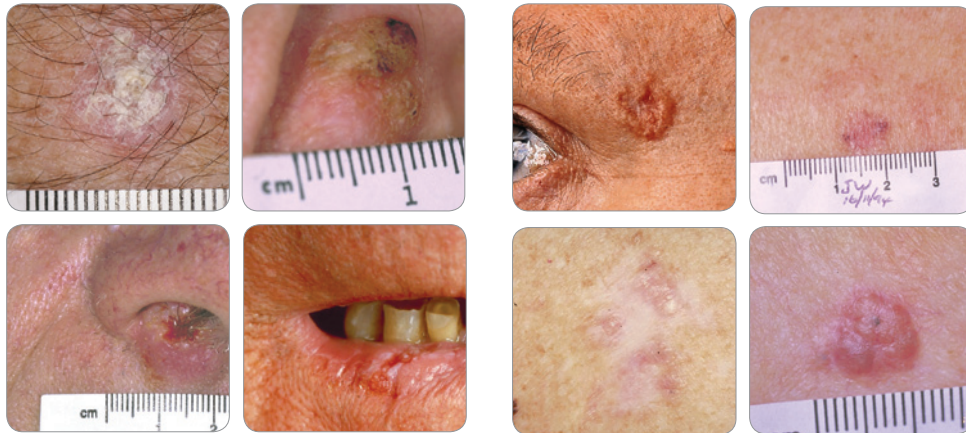
Non-melanoma skin cancer (NMSC) diagnosis

Squamous cell carcinoma (SCC)

- SCC can spread to other parts of the body if not treated. Lesions on the ears and lips have a higher risk of metastasis.
- It appears as a thickened, red, scaly nodule that may bleed and ulcerate over time.
- It grows over a period of some months. Rapid growth is associated with increased risk of mortality.

Basal cell carcinoma (BCC)

- BCC is the most common and least dangerous form of skin cancer.
- It appears as a well-defined lump or scaly area that is red or pearly in colour.
- It may bleed or become ulcerated early on, then heal and break down again.
- It usually grows relatively slowly.



Specialised melanoma and non-melanoma diagnosis and treatment services

Sydney Melanoma Diagnostic Centre	2nd Floor Gloucester House Royal Prince Alfred Hospital Camperdown NSW 2050	9515 8537	Diagnosis and management of melanoma and pigmented lesions
Melanoma Institute Australia	40 Rocklands Road North Sydney NSW 2060	9911 7200	Diagnosis, surgical management and medical treatment of melanoma
Calvary Mater Newcastle	Cnr Edith and Platt Streets Waratah NSW 2298	4985 0100	Diagnosis, surgical management and medical treatment of melanoma
Skin & Cancer Foundation Australia	277 Bourke Street Darlinghurst NSW 2010 7 Ashley Lane Westmead NSW 2145	8353 3000 8833 3000	Diagnosis and surgical management of melanoma and NMSC

Treatment for NMSC

Treatment options for non-melanoma skin cancer include:

- Surgical excision of the tumour and surrounding tissue
- Radiotherapy
- Cryotherapy
- Curettage
- Diathermy/electrodesiccation
- Application of topical agents (imiquimod cream, diclofenac gel, fluorouracil cream, photodynamic therapy).

The choice of treatment will depend on:

- Tumour size
- Thickness and grade
- Aetiology
- Histological features
- Anatomic site
- Patient preference.

Follow-up for NMSC

Frequency of follow-up of patients treated for NMSC for evidence of recurrence, metastasis and/or any new primary skin cancers will depend on histological clearance and risk level of tumour. Patients should be educated on recognising changes in their skin (including examination of draining lymph nodes for patients with SCC), have a professional full skin examination as deemed appropriate, and have further testing as required.

Clinical Practice Guide: Basal cell carcinoma, squamous cell carcinoma (and related lesions) – a guide to clinical management in Australia.
www.cancer.org.au

Screening for melanoma and NMSC

There is no evidence demonstrating that population-based screening for melanoma and NMSC 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 NMSC, including patients with a previous diagnosis of melanoma.

Skin self-examination (SSE) for melanoma and NMSC

Approximately 50% of melanomas are detected by the patient. There is no specific SSE technique or recommended frequency of self-examination that has 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 to 12 months.

Patients treated for NMSC should:

- Be taught to self-screen and recognise changes to their skin
- Have a full body examination with a clinician every 12 months.

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.

Cancer Council Helpline 13 11 20