Cancer Council WA

MELANOMA AND OTHER SKIN CANCERS: A GUIDE FOR MEDICAL PRACTITIONERS

Australia has among the highest rates of skin cancer in the world. Two in three 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 melanocyte (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 WA in 2017:

- There were more than 1,400 new cases of melanoma (11% of all cancer diagnoses) and over 130 deaths.
- Men over the age of 40 were more than one and a half times more likely to be diagnosed with melanoma and more than twice as likely to die from it, compared to women of similar age.
- The lifetime risk of developing melanoma by age 85 years was one in 21 for men and one in 30 for women.

Non-melanocytic skin cancer (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, dorsum 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. SCCs may 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. It can be found most commonly on the head and neck but also on the trunk and limbs. It can also be found in areas not exposed to sunlight.

In WA in 2014, there were 83,151 paid Medicare services for NMSC, and 82 deaths.

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 and skin cancer.
- An intermittent exposure pattern carries the highest risk for developing melanoma and BCC. UV exposure in adulthood or childhood contributes to BCC and melanoma risk.
- Actinic keratoses 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 (e.g. arsenic); radiation therapy and psoralen (PUVA) treatment for psoriasis; immunosuppressive therapy; and some rare genetic conditions predisposing people to skin cancer (e.g. Xeroderma pigmentosum, albinism).

Risk factors for melanoma

- Multiple naevi (moles)
- Multiple dysplastic naevi
- Personal or family history of melanoma
- Increasing age
- High levels of intermittent sun exposure (e.g. during outdoor recreation)
- Occupational sun exposure
- Personal history of NMSC
- Fair skin that burns easily, freckles and does not tan
- Fair or red hair and blue or green eyes
- Immune suppression and/or being a transplant recipient.

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 more than twice as likely to die from it.

The mortality rate for males aged 50–80 years is two to three times that of females.

Melanoma in Indigenous Australians and non- Caucasian patients

The incidence of melanoma in Indigenous Australians is low. For the period 2008–2012, twenty-two Indigenous Australians died from melanoma, representing 0.4% of all melanoma deaths. For the same period, there were 7,300 deaths from melanoma overall. 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 that are rare in Caucasian populations:

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

WA Kirkbride MELANOMA ADVISORY SERVICE

Melanoma diagnosis

Superficial spreading melanoma (SSM)

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

- SSM is the most common form of melanoma.
- SSM can appear as a new spot or as a change in the size, colour or shape of an existing mole.
- A patient diagnosed with SSM is at increased risk of developing a new primary melanoma.

Nodular melanoma (NM)

This is a dangerous form of melanoma that can metastasise early. It differs from SSM in appearance.

- NM has no 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 sun-damaged skin and in older people, particularly men.
- Approximately 10–15% of total melanomas diagnosed are NM.

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 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 e.g. itch).

The ABCDE acronym cannot be used to aid diagnosis of NM but the following features EFG – can assist with the diagnosis

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.

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.

Lentigo Maligna (LM)

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

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.

Diagnosis tools

Dermoscopy uses a hand-held magnifying device to allow the visualisation of diagnostic features of skin lesions that are not seen with the naked eye. It increases diagnostic accuracy and reduces unnecessary excision of benign lesions. Training in dermoscopy is recommended for clinicians routinely involved in skin cancer treatment.

- 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 changes and is useful in high-risk patients or patients with dysplastic naevus syndrome.
- In vivo confocal microscopy allows non-invasive “optical biopsy” with the visualisation of the morphology and organisation of the cells in deeper layers of the skin. It is useful for difficult diagnoses and margins (i.e. amelanotic melanoma, LM) and is used in specialised centres.

Smartphone applications for pigmented lesions

Melanoma apps are smartphone applications that assess risk of pigmented lesions using a smartphone camera and underlying algorithm. None of the melanoma apps tested have shown high enough agreement with a specialist clinical opinion to be considered adequate for assessing high-risk pigmented lesions.

Treatment for melanoma

Appropriate primary treatment will depend on the Breslow thickness of the tumour.

Tis - Melanoma in situ.	Melanoma cells are found only in the non-vascular epidermis and have not penetrated into the dermis.
T1	The melanoma is less than 1 mm thick.
T2	The melanoma is between 1 mm and 2 mm thick.
T3	The melanoma is between 2 mm and 4 mm thick.
T4	The melanoma is more than 4 mm thick.

- The T1-T4 (Primary Tumour Thickness) classification is further divided into groups depending on presence of ulceration (a or b).
  - Treatment is based on tumour thickness and involves the removal of the melanoma with a margin of excision based on the Tis-T4 classification.

Tis	5 mm clearance
T1 - T3	1 cm clearance
T4	*Consider a* 2 cm clearance

Note:

The optimal excision margin for melanoma 2–4 mm thick is debated. There is currently no evidence to support a clinical excision margin over 1cm for these lesions.

Discussion about sentinel lymph node biopsy (SLNB) is now considered the standard of care for all lesions >T1b (over 0.8mm Breslow thickness). SLNB may not be offered to patients who have had their lesion excised with a wide margin. Definitive excision of these lesions should not be performed before the patient has discussed SLNB with a surgeon who performs this procedure.

Flap reconstruction interferes with lymphatic drainage and should not be undertaken if SLNB has not been discussed with suitable patients (>T1b).

If a partial biopsy has been performed and the Breslow thickness is under 0.8mm, excision of the remaining lesion with a 2mm margin should be performed before definitive treatment of the lesion, in case a Breslow thickness over 0.8mm is confirmed. In this case, SLNB would then need to be discussed.

Other treatment options

Surgery

- Sentinel lymph node biopsy (SLNB) should be discussed with all patients with lesions over T1b (>0.8mm). These patients should be discussed at a multidisciplinary melanoma meeting such as the Western Australian Kirkbride Melanoma Advisory Service (WAKMAS) before definitive treatment is undertaken.
- Resection of isolated metastases can be performed in both therapeutic and palliative settings.

Radiation

- Radiotherapy may be considered as adjuvant treatment where the lesion has a high risk of local recurrence (e.g. Desmoplastic melanoma)
- Radiotherapy may be used for palliative management of cerebral and bone metastases and for other metastatic lesions where systemic treatment has failed.

Oncology treatments

- **Systemic treatment** is now available for patients with metastatic (including positive SLNB) or inoperable melanoma. Survival in patients with metastatic disease 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 (in particular the development of squamous cell carcinomas and minor skin disruptions). The current BRAF inhibitors used for targeted therapies include Dabrafenib and Vemurafenib. These are combined with MEK inhibitors (Trametinib and Cobimetinib respectively) to reduce toxicities and improve efficacy.
  - ***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 (possible side-effects include fatigue, arthralgia, joint pain and major autoimmune disease).
  - Current immunotherapy drugs in use include Nivolumab, Ipilimumab and Pembrolizumab. The first two may be used in combination therapy to increase efficacy whilst Pembrolizumab is used as monotherapy.

Trials for combination therapy and monotherapy of these drugs and new drugs for different stages of melanoma are ongoing and are constantly being introduced. For information on trials that may be available for your patients with advanced stage 2 disease (melanoma greater than 2.0mm thick with ulceration or over 4.0mm thick), please contact WAKMAS.

Follow-up for melanoma

Due to the risk of tumour recurrence and new primary melanomas, all patients require regular follow-up, as follows:

- 6-monthly intervals for 5 years then yearly for patients with insitu disease
- 3- 4-monthly intervals for 3 years, then 6 monthly until 5 years, and yearly follow-up thereafter for patients with invasive lesions.
- 3 monthly intervals for patients with metastatic disease
- *Patients who have had a positive SLNB who have not tolerated adjuvant treatment or who do not have adjuvant treatment should have 3-4 monthly ultrasound scans of the affected lymph node basin 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.

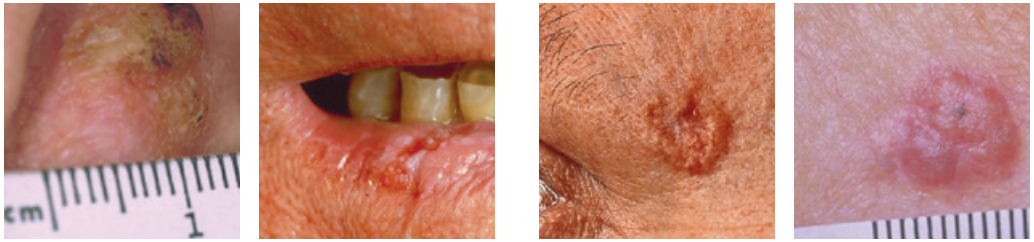
Non-melanoma skin cancer (NMSC) diagnosis

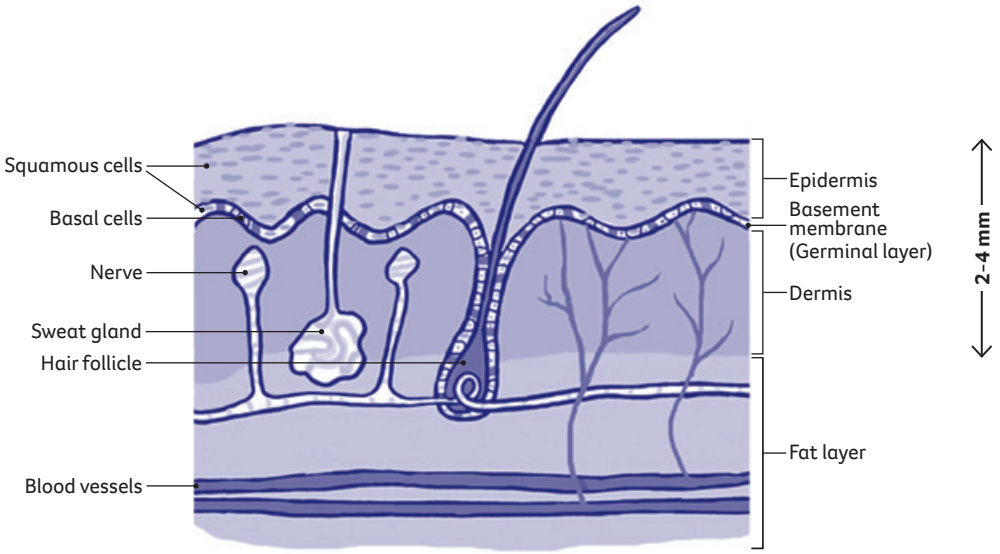
Squamous cell carcinoma (SCC)

- SCC can spread to other parts of the body if not treated. Lesions on the 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 and may be painful.

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 appearance.
- BCC may bleed or become ulcerated early on, then heal and break down again.
- BCC usually grows relatively slowly.
- High-risk BCC subtypes (eg micronodular, infiltrating or morphoeic) and BCCs inimmune suppressed individuals tend to have higher rates of recurrence after treatment.





Treatment for NMSC

Treatment options for NMSC include:

- surgical excision of the tumour and surrounding tissue
- radiotherapy
- curettage and electrodesiccation for larger lesions on the trunk.

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 anatomic site
- Patient preference, age and medical comorbidities.

A course on skin biopsy procedures is available for GPs, for more information please contact The Royal Australian College of General Practitioners (RACGP).

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 the tumour. 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 examination of draining lymph nodes for patients with SCC).

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.

Skin surveillance is recommended for patients identified as high risk for 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 been shown to reduce morbidity. However, regular skin examination may increase the probability of detecting skin cancer at an early and treatable stage.

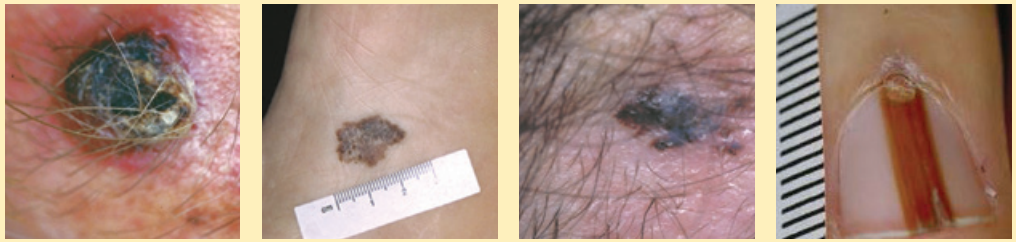
Patients at high risk for melanoma should be taught to self-screen (including examination of draining lymph nodes) and recognise suspicious lesions. They should have a full body examination with a clinician every 6 to 12 months.

Patients treated for NMSC should be taught to self-screen and recognise changes to their skin. They should have a full body examination with a clinician every 6-12 months or more frequently for patients at higher risk.

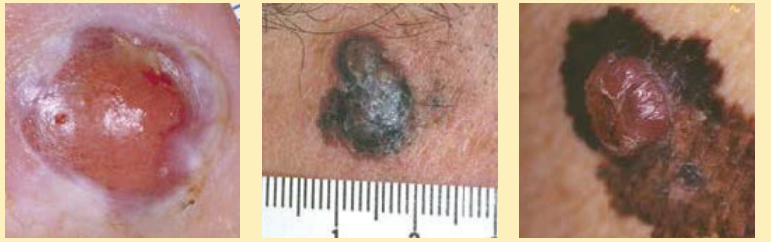
For the general population, the Australasian College of Dermatologists recommends SSE 4 times a year or as often as recommended by their medical practitioner.

Image references

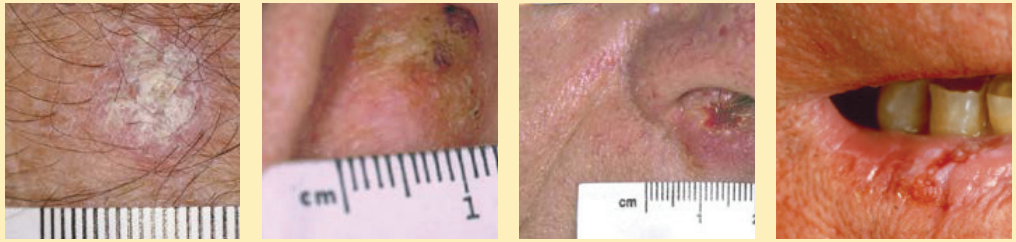
Superficial spreading melanoma (SSM)



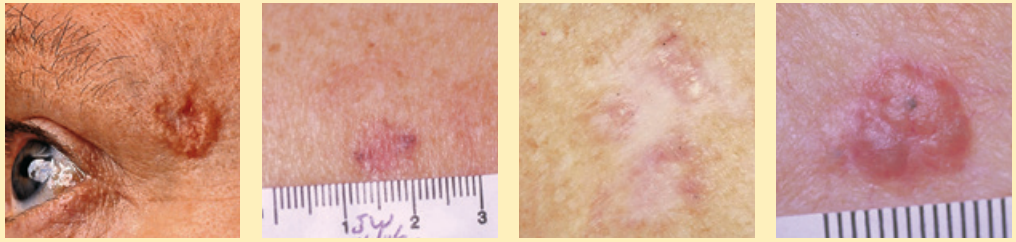
Nodular melanoma (NM)



Squamous cell carcinoma (SCC)



Basal cell carcinoma (BCC)



Images are supplied courtesy of the Sydney Melanoma Diagnostic Centre.

Key references

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Specialised melanoma and non-melanoma advisory services

> **The Australasian College of Dermatologists** website provides a "Find a Dermatologist" search function to assist in finding Dermatologists by location.
dermcoll.edu.au

> **Western Australian Kirkbride Melanoma Advisory Service (WAKMAS)**
Comprehensive advice from a multidisciplinary panel of specialists regarding the management of complex, advanced and metastatic malignant melanoma.
Harry Perkins Institute of Medical Research
6 Verdun St, QEII Medical Centre, Nedlands
T. 08 6151 0860 F. 08 6151 1032
wakmas@perkins.org.au
wakmas.org.au

> **The Australian Society of Plastic Surgeons** website provides a "Find a Surgeon" search function to assist in finding plastic surgeons by location.
p: 02 9437 9200 | f: 02 9437 9210
info@plasticsurgery.org.au
plasticsurgery.org.au

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