

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 in their lifetime.

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. More common clinical subtypes of melanoma include:

- Superficial spreading melanoma (SSM) accounts for approximately 55-60% of melanomas disgnosed. 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 UV radiation.
- Nodular melanoma (NM) accounts for approximately 10-15% of melanomas diagnosed. It is important to be aware of this subtype of melanoma because they grow rapidly and invade early.
- Lentigo maligna melanoma (LMM) accounts for approximately 10-15% of melanomas.

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.
- 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.

Causes of skin cancer

- Unprotected exposure to UV radiation (UVA and UVB)
 - The single most important lifestyle risk factor.
 - All people should be advised to use sun protective measures when UV levels are >3.
 - Outdoor workers should use sun protective measures when outdoors for extended periods, regardless of UV levels.
 - Contributes to skin damage and premature ageing.
- An intermittent sun exposure pattern (in childhood or adulthood) carries the highest risk for developing melanoma and BCC.
- Sun exposure accumulated over a lifetime is associated with actinic keratoses and SCC.

Risk factors for skin cancer

- Having fair skin (Fitzpatrick 1-2)
- Having light or red hair colour
- Having freckles or light eye colour
- A family history of skin cancer (melanoma and SCC)
- A personal history of skin cancer
- Increasing age
- Occupational sun exposure
- Being immune suppressed, especially amongst organ transplant recipients
- Additionally, at higher risk of melanoma are those with:
 - Over 50 naevi (moles)
 - Multiple dysplastic naevi
- High levels of intermittent sun exposure
- Other risk factors for NMSC include: - Radiation therapy

- Exposure to some chemicals (e.g., arsenic)
- Psoralen (PUVA) treatment for psoriasis
- Rare genetic conditions predisposing people to skin cancer (e.g., xeroderma pigmentosum, albinism).

Gender

Men are more likely to be diagnosed and die from melanoma than women. Mortality from melanoma rises for men from 40 years and continues to increase with age. In WA in 2019, men were one and a half times as likely to be diagnosed with melanoma and 2.5 times as likely to die from it, compared to women.

Aboriginal and Torres Strait Islander peoples and other non-Caucasians

The incidence of melanoma in Aboriginal and Torres Strait Islander peoples is low, representing 0.5 per cent of all melanoma deaths from 2015 to 2019.

The incidence of melanoma in non-Caucasians is also low; however, this population 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, such as:

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



Burden and impact in WA

- In 2019, there were more than 1,500 new cases of melanoma (11% of all cancer diagnoses) and over 140 deaths from melanoma.
- In 2019, the lifetime risk of developing melanoma by age 75 years was one in 21 for men and one in 30 for women.
- There were 120,032 paid Medicare services for NMSC in 2021.
- In 2020, there were 72 deaths from NMSC.

Melanoma diagnosis

Superficial spreading melanoma (SSM)

- The most common form of melanoma.
- 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.
- NM has no radial growth within the epidermis but penetrates vertically into the dermis early.
- NM can develop de novo in normalappearing skin or within another type of melanoma.
- Differs from SSM in appearance. Is more likely to be symmetrical and uniform in colour (red, pink, brown or black), lighter coloured, and firm to the touch. Over time, it may develop a crusty surface that bleeds easily.
- Develops most commonly on sun-damaged skin and in older people, particularly men.

Lentigo maligna (LM)

- Slow-growing form of melanoma in situ that can be difficult to recognise.
- Commonly found at sites of frequent sun exposure, such as the head and neck.
- Incidence is increasing.
- Margin determination can be challenging and local recurrence is more common than in other types of melanoma.

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

Asymmetry: the lesion is irregular in shape or pattern.

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

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G

Colour: there is variation in colour within the lesion.

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). This is the most important clinical indicator of melanoma.

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

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.

Firm: the lesion feels firm to the touch when palpated.

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.

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 GPs 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 highrisk patients or patients with dysplastic naevus syndrome.
- In vivo confocal microscopy allows noninvasive "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

Smartphone melanoma applications ('apps') are widely available and claim to assess risk of pigmented lesions using the smartphone camera and an underlying algorithm. None of the melanoma apps tested have shown high enough agreement with a specialist clinical opinion to be considered adequate for assessing pigmented lesions.

Treatment for melanoma

Appropriate primary treatment will depend on the Breslow thickness of the tumour and involves the removal of the melanoma with a margin of excision based on the primary tumour thickness (Tis-T4) classification.

Primary tumour thickness classification	Breslow thickness	Clinical margin
Tis - Melanoma in situ	Melanoma cells are found only in the non-vascular epidermis and have not penetrated into the dermis.	5mm clearance
т1	Less than 1 mm thick.	10mm clearance
т2	Between 1mm and 2mm thick.	10-20mm clearance*
тэ	Between 2mm and 4mm thick.	
τ4	More than 4mm thick.	Consider a 20mm clearance*

Notes:

The primary tumour thickness classification is further divided into groups (a or b) depending on the presence of ulceration.

*The optimal excision margin for melanoma 2–4 mm thick is debated. There is currently no evidence to support a clinical excision margin over 10mm for these lesions.

Discussion about sentinel lymph node biopsy (SLNB) is 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. SLNB would then need to be discussed.

Other treatment options

Surgery

- 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 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.

Follow-up for melanoma

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

- 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 professional full skin examinations, and have further testing as required. Information on self-checks for skin cancer is available at: www.myuy.com.au/skincancer/

Trials of 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 including those with advanced stage 2 disease, please contact the <u>Western Australian Kirkbride Melanoma Advisory Service (WAKMAS)</u>.

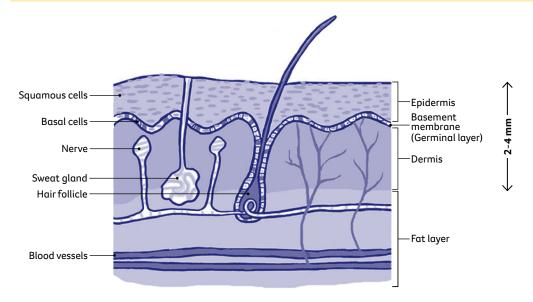
Non-melanocytic skin cancer (NMSC) diagnosis

Squamous cell carcinoma (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.
- Appears as a thickened, red, scaly nodule that may bleed and ulcerate over time.
- Grows over a period of weeks to months and may be painful.

Basal cell carcinoma (BCC)

- The most common and least dangerous form of skin cancer.
- Appears as a well-defined lump or scaly area that is red or pearly in appearance.
- May bleed or become ulcerated early on, then heal and break down again.
- 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.



Treatment for NMSC

- Surgical excision of the tumour and surrounding tissue.
- Radiotherapy.
- Curettage and electrodesiccation for larger lesions on the trunk.
- For biopsy-proven superficial lesions:
 - Cryotherapy
 - Topical agents including 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.

Follow-up for NMSC

For patients who have been treated for NMSC, the frequency of their follow up (for evidence of recurrence, metastasis, and/or any new primary skin cancers) will depend on histological clearance and the 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, for patients with SCC, examination of draining lymph nodes).

Screening for melanoma and NMSC

Population-based screening for melanoma or NMSC is not recommended as there is insufficient evidence available to show that this reduces morbidity and mortality.

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 selfexamination 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 very high risk for melanoma

should be taught to self-screen (including examination of draining lymph nodes) and to recognise suspicious lesions. These individuals should be checked regularly by a clinician with six-monthly full skin examination supported by total body photography and dermoscopy

Patients treated for NMSC should be taught to self-screen and recognise changes to their skin. (including, for patients with SCC, examination of draining lymph nodes).

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

Images of different skin cancer types

Superficial spreading melanoma (SSM)



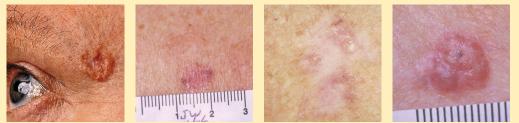
Nodular melanoma (NM)



Squamous cell carcinoma (SCC)



Basal cell carcinoma (BCC)



Images are supplied courtesy of the Sydney Melanoma Diagnostic Centre.

Specialised melanoma and non-melanoma advisory services

- > Western Australian Kirkbride Melanoma Advisory Service (WAKMAS) provides 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
 E: wakmas@perkins.org.au
 wakmas.org.au
- > The Australasian College of Dermatologists website provides a "Find a Dermatologist" search function to assist in finding Dermatologists by location. <u>dermcoll.edu.au</u>
- The Australian Society of Plastic Surgeons website provides a "Find a Surgeon" search function to assist in finding Plastic Surgeons by location.
 T: 02 9437 9200 | F: 02 9437 9210
 E: info@plasticsurgery.org.au
 plasticsurgery.org.au

Key references

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