

Cancer Association of South Africa (CANSA)



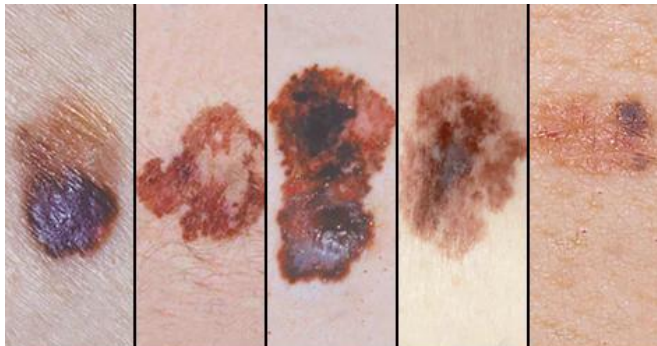
CANSA Fact Sheet on Melanoma

Introduction

Melanoma, the most serious type of skin cancer, develops in the cells (melanocytes) that produce melanin — the pigment that gives your skin its colour.

[Picture Credit: Melanoma of the Skin]

Melanoma can develop anywhere on the body, including the head and neck, the eyes, the skin under the fingernails, the genitals, and even the soles of the feet or palms of the hands.



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Melanoma can develop anywhere on the body, including the head and neck, the eyes, the skin under the fingernails, the genitals, and even the soles of the feet or palms of the hands. Melanoma may not be coloured like a mole. It may have no colour or be slightly red, which is called amelanotic melanoma.

Melanoma most often develops in areas that have had exposure to the sun, such as your back, legs, arms and face. Melanomas can also occur in areas that don't receive much sun exposure, such as the soles of your feet, palms of your hands and fingernail beds.

Melanoma can show up inside the body too. That is because melanomas arise from cells (melanocytes) that are naturally found all over the body. Internal melanomas include:

Mucosal melanoma - It can develop in the mucosal tissues that line the nose, mouth, oesophagus, anus, urinary tract and vagina.

Desmoplastic melanoma - a form of melanoma that is usually found on skin that contains high amounts of cumulative skin damage on the head and neck. It accounts for approximately 1% of all melanomas

Uveal melanoma - a form of melanoma found in the eyes that may cause vision impairment and loss, among other issues. Early symptoms of uveal melanoma are rare and often discovered during routine

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eye exams. Later symptoms may include dark spots in the eyes, blurred vision, floaters, and changes to the eye shape and position.

Amelanotic melanomas – are missing the dark pigment melanin that gives most moles their colour. Amelanotic melanomas may be pinkish, reddish, white, the colour of one's skin or even clear and colourless, making them difficult to recognise.

Acral lentiginous melanoma – the most common form of melanoma found in people of colour, often appears in hard-to-spot places, including under the fingernails or toenails, on the palms of the hands or soles of the feet.

Superficial spreading melanoma - is a type of skin cancer that grows horizontally in upper layers of the skin and eventually into deeper layers of the skin. It is the most common type of melanoma, accounting for about 70% of all diagnosed melanomas. Symptoms and traits to look out for include:

- raised or flat shape, often with irregular shape and borders, sometimes on an existing or new mole
- brown, black, tan, red, blue, and even white, often a darker shade of a person's normal skin tone
- slow changes, often over the course of months or years

Nodular melanoma - is one of the most aggressive forms of skin cancer. Symptoms and traits to look out for include:

- a hard, raised bump
- blackish-blue, dark brown, or reddish blue in colour (sometimes the same tone as the skin)
- continuously growing in size and shape, especially after 2 to 3 weeks

Hutchinson's melanotic freckle - is an invasive skin cancer that develops out of lentigo maligna, a type of melanoma in situ. This means that it's not cancerous and isolated just to the upper layers of the skin. This type of melanoma can become cancerous and turn into Hutchinson's melanotic freckle, or lentigo maligna melanoma. Symptoms and traits to look out for in a skin spot include:

- a large flat or slightly raised brown or black patch, similar to an age spot or freckle
- having a smooth surface and irregular shape
- having a brown hue, though it can also be red, pink, or white on occasion, depending on skin tone
- a larger patch, usually at least 6 millimetres

Melanomas are grouped into the following stages:

- **Stage 0 (Melanoma in situ):** The melanoma is only in the top layer of skin (the epidermis).
- **Stage I:** Low-risk primary melanoma with no evidence of spread. This stage is generally curable with surgery.
- **Stage II:** Features are present that indicate higher risk of recurrence, but there is no evidence of spread.
- **Stage III:** The melanoma has spread to nearby lymph nodes or nearby skin.
- **Stage IV:** The melanoma has spread to more distant lymph nodes or skin or has spread to internal organs.

Melanoma can affect all ethnic and racial groups; however, the typical melanoma patient has a fair complexion and a tendency to sunburn rather than tan, even after a brief exposure to sunlight. Although there is no conclusive evidence that exposure to sunlight is causally related to the development of melanoma, lesions are most commonly found on sun-exposed areas of the body.

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Other epidemiologic risk factors include the occurrence of a previous melanoma and an afflicted first-degree relative (parent or sibling).

Although anyone can develop melanoma, an increased risk for developing the disease is seen in people with:

- A personal history of melanoma;
- A family history of melanoma;
- Fair skin, freckles, blond or red hair and blue eyes;
- Excess sun exposure, including blistering sunburns;
- An address near the equator or in high elevations — living in these locations may increase your UV exposure;
- A history of tanning bed use;
- Many moles, especially atypical moles; and
- A weakened immune system.

The exact cause of all melanomas is not clear, but exposure to ultraviolet (UV) radiation from sunlight or tanning lamps and tanning beds increases one's risk of developing melanoma. Limiting one's exposure to UV radiation can help reduce the risk of melanoma.

The risk of melanoma seems to be increasing in people under 40, especially women. Knowing the warning signs of skin cancer can help ensure that cancerous changes are detected and treated before the cancer has spread. Melanoma can be treated successfully if it is detected early. (NHS UK, 2023).

Tasdogan, A., Sullivan, R.J., Katalinic, A., Lebbe, C., Whitaker, D., Puig, S., V van de Poll-Franse, L., Massi, D. & Schadendorf, D. 2025.

"Cutaneous melanoma is a common cancer in Australia and New Zealand, Europe, and North America, and its incidence is still increasing in many regions. Ultraviolet (UV) radiation exposure (for example, through excessive sunlight exposure) remains the primary risk factor for melanoma; however, public awareness campaigns have led to a marked reduction in mortality. In addition to genetic damage from UV radiation, specific genetic alterations have been linked to melanoma. The stage of the tumour at the time of diagnosis is of greater importance for melanoma prognosis than in almost any other cancer. Context-dependent genetic mutations that attenuate tumour-suppressive mechanisms or activate growth-promoting signalling pathways are crucial factors in the development of cutaneous melanoma. In addition to external factors such as UV radiation, the tumour microenvironment can contribute to melanoma progression, invasion and metastasis. Cutaneous melanoma treatment has improved considerably over the past decade with the discovery and development of immune checkpoint inhibitors and therapy targeting BRAF and MEK. Over the next decade, several priorities are likely to influence melanoma research and management, including the continued advance of precision medicine methods to identify the most suitable patients for the most effective treatment, with the aim of improving clinical outcomes."

Conflict of interest statement

Competing interests: A.T. declares speakers' honoraria from Merck Sharp & Dohme. R.J.S. declares personal fees from Marengo, Merck, Novartis, Pfizer and Replimune for consulting/advisory board activity, and research grant support to his institution from Merck. C.L. declares conflicts of interest with BMS, Pierre Fabre, Sanofi, Novartis, MSD, Amgen, Merck Serono, Roche, Influx and Pfizer. S.P. declares research grants from Almirall, Pfizer, Regeneron, Sanofi, La Roche Posay, Philogen, ISDIN and International School of Derma; consulting fees from Sanofi, Regeneron, ISDIN, L'Oreal, La Roche Posay and International School of Derma; personal fees from Sanofi, Sunpharma, Cantabria, Eucerin, ISDIN, L'Oreal, La Roche Posay, Almirall, Avene and Pierre Fabre; and support for attending meetings and/or travel from Almirall, Cantabria and ISDIN. D.M. declares personal fees from Novartis, Sun Pharma, Bayer HealthCare Pharmaceuticals Inc., Pierre-Fabre Oncology, Sanofi

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Mogensen, M., von Knorring, T., Hölmich, L.R., Steiniche, T., Lade-Keller, J., Karmisholt, K. & Omland, S.H. 2025.

“Melanoma incidence is rising worldwide and has doubled in Denmark over the past 25 years. Early detection is essential but challenging due to difficulties in diagnosing early melanomas and atypical nevi. This review discusses melanoma diagnostic processes in the Danish healthcare system, highlighting current and emerging diagnostic tools. More accurate methods are needed to improve diagnosis and minimise unnecessary excisions. Although AI shows promise in this area, it has not yet surpassed the expertise of experienced dermatologists. Public education about mole changes remains crucial, as many melanoma cases are self-detected.”

Sun, Y., Shen, Y., Liu, Q., Zhang, H., Jia, L., Chai, Y., Jiang, H., Wu, M. & Li, Y. 2025.

Background: Melanoma, a significant global health concern, has shown evolving epidemiologic trends. Accurate estimation of melanoma's burden is essential for public health strategies and interventions.

Objectives: This study aims to estimate the incidence, mortality, and disability-adjusted life years for melanoma, stratified by region, gender, and age group, from 1990 to 2021.

Methods: Using data from the Global Burden of Disease 2021, we analyzed melanoma incidence, mortality rates, and disability-adjusted life years in 204 countries from 1990 to 2021. These metrics were age-standardized and stratified by age, sex, Socio-Demographic Index, region, and country. The estimated annual percentage change was calculated to track temporal trends.

Results: Our study shows a substantial global increase in melanoma incidence, with significant disparities between genders and age groups. Higher Socio-Demographic Index regions had increased incidence rates, while global mortality declined, likely due to improved detection and treatment.

Limitations: The reliance on estimates and models may introduce bias due to variability in disease definitions, diagnostic criteria, and data collection methods.

Conclusion: This study underscores the dynamic nature of melanoma's burden and the need for targeted, age-specific, and gender-specific interventions. Continued research is essential to address the growing challenges posed by melanoma.

Conflict of interest statement

Conflicts of interest None disclosed.

The International Classification of Disease 10th Version (ICD-10)

The International Classification of Diseases (ICD) is designed to promote international comparability in the collection, processing, classification, and presentation of mortality statistics. This includes providing a format for reporting causes of death on the death certificate.

ICD serves a broad range of uses globally and provides critical knowledge on the extent, causes and consequences of human disease and death worldwide via data that is reported and coded with the ICD. Clinical terms coded with ICD are the main basis for health recording and statistics on disease in primary, secondary and tertiary care, as well as on cause of death certificates. These data and statistics support payment systems, service planning, administration of quality and safety, and health services

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research. Diagnostic guidance linked to categories of ICD also standardizes data collection and enables large scale research.

For more than a century, the International Classification of Diseases (ICD) has been the basis for comparable statistics on causes of mortality and morbidity between places and over time. Originating in the 19th century, the latest version of the ICD, ICD-11, was adopted by the 72nd World Health Assembly in 2019 and came into effect on 1st January 2022.

The ICD-10 Code for malignant melanoma of the skin – C43.9.
(World Health Organization, 2025).

Tumour Grade vs Tumour Stage

A cancer's grade describes how abnormal the cancer cells and tissue look under a microscope when compared to healthy cells. Cancer cells that look and organise most like healthy cells and tissue are low grade tumours. Doctors describe these cancers as being well differentiated. Lower grade cancers are typically less aggressive and have a better prognosis.

While a grade describes the appearance of cancer cells and tissue, a cancer's stage explains how large the primary tumour is and how far the cancer has spread in the patient's body.

There are several different staging systems. Many of these have been created for specific kinds of cancers. Others can be used to describe several types of cancer.

One common system that many people are aware of puts cancer on a scale of 0 to IV.

- Stage 0 is for abnormal cells that haven't spread and are not considered cancer, though they could become cancerous in the future. This stage is also called "in-situ."
- Stage I through Stage III are for cancers that haven't spread beyond the primary tumour site or have only spread to nearby tissue. The higher the stage number, the larger the tumour and the more it has spread.
- Stage IV cancer has spread to distant areas of the body.

(University of Texas, MD Anderson Cancer Center. 2025).

Other Forms of Skin Cancer

The following pictures may assist to differentiate between melanoma of the skin and other forms of skin cancer:



[Picture Credit: Other Forms of Skin Cancer]

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Incidence of Melanoma of the Skin

According to the latest edition of the National Cancer Registry (2023) the following cases of skin cancer were histologically diagnosed in South Africa during 2023. In the case of melanoma, it must be pointed out that all cases of melanoma (no matter where in the body it occurred) are grouped together:

Group 2023	Type of Skin Cancer	Actual Number of Cases	Estimated Lifetime Risk	Total of All Cancers
All Males	Basal Cell Carcinoma	8 191	1:25	19,64%
All Females		6 568	1:47	14,23%
All Males	Squamous Cell Carcinoma	4 449	1:52	10,66%
All Females		3 323	1:110	7,20%
All Males	Melanoma (all forms)	1 179	1:186	2,82%
All Females		1 111	1:279	2,41%

The Role of BRCA Gene Mutation

BRCA is an abbreviation originating from **Br**(east) **Ca**(ncer) and are tumour suppressor genes. Every cell in a human body contains them. There are two types: BRCA1 and BRCA2. Their main function in the body is to repair DNA, keep other genes healthy, and prevent cancerous changes. These genes can become mutated.

A mutation is a change in the gene which makes the gene stop doing its main function, therefore, no longer keeping abnormal cell growth in check. These changes (mutations) can be inherited or passed on from parents, grandparents, and great grandparents.

If someone has a gene mutation, their risk of cancer increases.

Anyone can have a BRCA gene mutation. Though, they are more commonly found in certain ethnic groups, including Ashkenazi Jews, Afrikaners, French Canadians, and people of Icelandic backgrounds. The most common cancers that can result from BRCA gene mutations are breast cancer, ovarian cancer, and prostate cancer. The full list includes.

Women

BRCA1

Breast cancer
Ovarian cancer
Pancreatic cancer

BRCA2

Breast cancer
Ovarian cancer
Pancreatic cancer
Melanoma

Men

BRCA1

Breast cancer
Prostate cancer
Pancreatic cancer

BRCA2

Breast cancer
Prostate cancer
Melanoma
Pancreatic cancer

If someone has a BRCA mutation, they may pass the mutation to their children. Each child has a 50% chance of inheriting their parents' BRCA gene mutation. One's siblings may also have inherited the BRCA gene mutation.

(National Breast Cancer Foundation, Inc., 2024; Northwestern Medicine, 2025).

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Signs and Symptoms of Melanoma

To help identify characteristics of unusual moles that may indicate melanomas or other skin cancers, think of the letters ABCDE:

- **A** is for asymmetrical shape. Look for moles with irregular shapes, such as two very different-looking halves.
- **B** is for irregular border. Look for moles with irregular, notched or scalloped borders — characteristics of melanomas.
- **C** is for changes in colour. Look for growths that have many colours or an uneven distribution of colour.
- **D** is for diameter. Look for new growth in a mole larger than about 6 millimetres.
- **E** is for evolving. Look for changes over time, such as a mole that grows in size or that changes colour or shape. Moles may also evolve to develop new signs and symptoms, such as new itchiness or bleeding.

Cancerous (malignant) moles vary greatly in appearance. Some may show all of the changes listed above, while others may have only one or two unusual characteristics.

The first sign of flat melanoma is usually a new spot or an existing mole or freckle that changes in appearance. Some changes can include:

- A spot that has grown in size (evolved)
- A spot where the edges are looking irregular versus smooth and even
- A spot that has a range of colours such as brown, black, blue, red, white or light grey
- A spot that has become itchy or is bleeding

The Ugly Duckling Sign

The **Ugly Duckling** is another warning sign of melanoma. This recognition strategy is based on the concept that most normal moles on your body resemble one another, while melanomas stand out like ugly ducklings in comparison. This highlights the importance of not just checking for irregularities but also comparing any suspicious spot to surrounding moles to determine whether it looks different from its neighbours. These ugly duckling lesions or outlier lesions can be larger, smaller, lighter or darker, compared to surrounding moles. Also, isolated lesions without any surrounding moles for comparison are considered ugly ducklings.

(Columbia University Herbert Irving Comprehensive Cancer Center, 2026).

Diagnosis of Melanoma

Melanoma is diagnosed by:

- physical examination – including medical history
- excision biopsy – under local anaesthetic, the suspected melanoma and some of the surrounding skin is removed. The sample will be examined in a laboratory for signs of cancer.

Test results can take a few days to come back. It is very natural to feel anxious waiting to get your results. It can help to talk to a close friend or relative about how you are feeling.

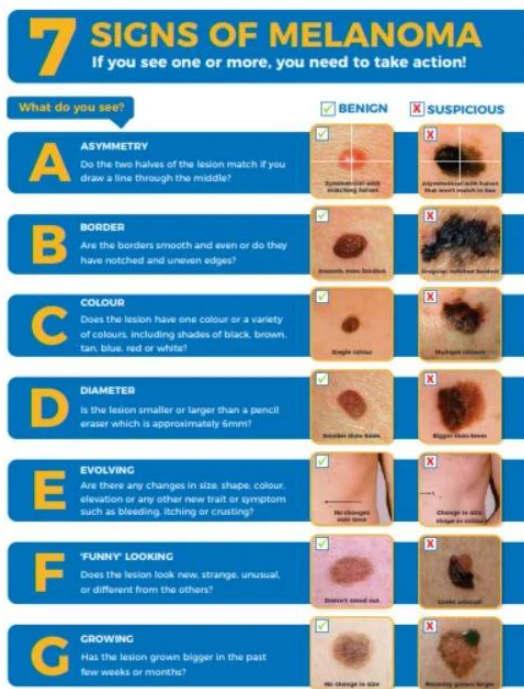
If a melanoma is diagnosed, further tests may be needed if surgery is planned or to see if the cancer has spread to other areas of the body. These tests may include:

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- Blood tests;
- Chest X-ray;
- Ultrasound scan;
- Magnetic Resonance Imaging (MRI) scan;
- Computed tomography (CT) scan;
- Bone scan; and
- Lymph node biopsy.

[Picture Credit: 7 Signs of Melanoma]

Laboratory tests

A dermatologist may also perform other tests to determine whether a melanoma is present. These are called immunohistochemistry (IHC) tests.

- Fluorescence in situ hybridization (FISH) maps the genetic material in a patient's cells and helps the physician to distinguish a benign nevus from a melanoma.
- Comparative genomic hybridization (CGH) further aids the physician in determining

whether or not melanoma is present.

The pathologist's report should include a macroscopic description of the specimen and melanoma (the naked eye view), and a microscopic description. The following features should be reported if there is invasive melanoma:

- Diagnosis of primary melanoma
- Breslow thickness to the nearest 0.1 mm
- Clark level of invasion
- Margins of excision i.e. the normal tissue around the tumour
- Mitotic rate – a measure of how fast the cells are proliferating
- Whether or not there is ulceration
- The report may also include comments about the cell type and its growth pattern, invasion of blood vessels or nerves, inflammatory response, regression and whether there is associated in-situ disease and/or associated naevus (original mole).

Breslow depth and Clark level of Melanoma

Breslow Depth

The Breslow Depth is a helpful measure of how far melanoma has invaded the body. Knowing the depth of melanoma is helpful because it is important when considering future treatment.

The Breslow Depth has been replaced by the American Joint Committee on Cancer (AJCC) staging system. The AJCC system assigns a stage based on tumour, node, metastasis (TMN) scores and other prognostic factors. The goal is that melanomas of the same stage will have similar characteristics, treatment options, and outcomes.

Clark Level

The Clark Level is a staging system that describes the depth of melanoma as it grows in the skin. The doctor may provide a level for the melanoma in addition to, or in place of, a stage. These designations are not interchangeable.

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The Clark Scale has five levels:

Level 1: Melanoma is confined to the epidermis (the outer layer of the skin)

Level 2: Melanoma has invaded the papillary dermis (the outermost layer of the dermis, the next layer of skin)

Level 3: Melanoma has invaded throughout the papillary dermis and is touching on the next, deeper layer of the dermis

Level 4: Melanoma has invaded this next deeper layer, the reticular dermis

Level 5: Melanoma has now invaded the fat under the dermis

(Melanoma Institute Australia, Dermatologist, 2026; Dana-Faber Cancer Institute, 2026; Melanoma (Research Alliance, No date).

Treatment of Melanoma

The main treatment for melanoma is surgery, although treatment will depend on circumstances. If melanoma is diagnosed and treated at an early stage, surgery is usually successful.

If melanoma is not diagnosed until an advanced stage, treatment is mainly used to slow the spread of the cancer and reduce symptoms. This usually involves medicines that target specific genetic changes in the melanoma, such as BRAF inhibitors, or medicines that boost your body's immune responses to the melanoma.

Once one has had melanoma, there is a chance it may return. This risk is increased if the cancer was more advanced or widespread.

Treatment of Melanoma of the skin includes:

- Surgery
- Lymphadenectomy
- Metastasectomy
- Radiation Therapy
- Immunotherapy
- Chemotherapy
- Targeted Therapy
- Clinical Trials

(Mayo Clinic, 2023; Cancer Research UK, 2025; Cleveland Clinic, 2021; Melanoma Research Alliance, No date; MD Anderson Cancer Center, 2026).

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

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The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: <https://pactr.samrc.ac.za/>

Summary for the Average Reader

Melanoma is the most dangerous form of skin cancer, originating in the pigment-producing cells called melanocytes. While it accounts for only about 1% of skin cancer cases, it causes the vast majority of skin cancer-related deaths due to its ability to spread rapidly to other organs.

Warning Signs: The ABCDE Rule

Dermatologists use the ABCDE acronym to identify suspicious moles or spots:

- A - Asymmetry: One half of the spot does not match the other.
- B - Border: The edges are irregular, ragged, notched, or blurred.
- C - Colour: The colour is uneven and may include shades of brown, black, tan, red, white, or blue.
- D - Diameter: The spot is larger than 6 mm (about the size of a pencil eraser), though some can be smaller.
- E - Evolving: The spot is changing in size, shape, colour, or elevation.

Other signs include the "Ugly Duckling" sign—a mole that looks different from all others on your body—or a sore that will not heal.

Common Types of Cutaneous Melanoma

- Superficial Spreading Melanoma: The most common type (70%); often grows along the skin surface before invading deeper.
- Nodular Melanoma: The most aggressive type; often appears as a firm, raised bump (blue-black or red) and grows downward quickly.
- Lentigo Maligna Melanoma: Typically found in older adults on chronically sun-damaged skin, such as the face.
- Acral Lentiginous Melanoma: Occurs in "hidden" areas like the palms, soles of the feet, or under nails. It is the most common form in people with darker skin tones.

Risk Factors and Prevention

- UV Exposure: The primary cause is DNA damage from ultraviolet radiation (sunlight or tanning beds).
- Personal Traits: High risk is associated with fair skin, light hair/eyes, a history of blistering sunburns, or having many moles (>50).
- Prevention: Use broad-spectrum sunscreen (SPF 30+), wear protective clothing, and avoid peak sun hours (10 a.m. to 4 p.m.).

Staging and Treatment

Treatment and survival depend heavily on the Breslow thickness (how deep the tumour has grown).

- Stages 0–II: Localized to the skin. Usually treated with surgical excision to remove the tumour and a margin of healthy skin.

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- Stages III–IV: Cancer has spread to lymph nodes or distant organs. Treatment may include immunotherapy, targeted therapy, radiation, or chemotherapy. (AI Overview, 2026).

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