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## **Prevention and early detection of the most aggressive skin cancer: melanoma**

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## **ABSTRACT**

### **Introduction and purpose**

Skin cancers are the most common cancers and they are divided into two types: melanoma and non-melanoma skin cancers (NMSCs). Melanoma is the most lethal and aggressive type of skin cancer. The incidence of this type of cancer is increasing. Mortality from melanoma can be reduced by avoidance of exposure to ultraviolet radiation and regular skin examination.

## **Materials and methods of research**

English-language scientific literature available in the PubMed and Google Scholar databases was reviewed using the following keywords: "melanoma"; "early-detection"; "self-screening"; "tanning"; "sunscreen"; "dermatoscopy"; "mortality"; "prevention"; "risk-factors"; "UV protection"; "epidemiology".

## **Aim of the study**

The purpose of this narrative review is to present risk factors, prevention and the importance of early detection of melanoma. This review also shows that it is possible to increase people's awareness of skin self-examination and the importance of UV protection through the use of modern technology (text messaging).

## **Conclusions**

There are many risk factors for melanoma. People's awareness of the risks of UV exposure from both sunbathing and tanning beds is increasing. More and more people are starting to protect themselves from the sun and regularly check their skin. This behavior reduces the risk of developing melanoma and increases the chances of detecting melanoma in its early stages.

**Keywords:** melanoma; early-detection; self-screening; dermatoscopy; risk-factors; UV protection

## **INTRODUCTION**

Melanoma is the most dangerous and lethal type of skin cancer. It develops from the melanin-producing cells known as melanocytes. Melanoma is most commonly found on the skin, but it can also occur in the mouth, bowel and eye. Approximately 25% of melanomas develop from moles. The incidence of melanoma is steadily increasing in the developed world and looks set to continue to rise. The term 'malignant melanoma' is often used for melanoma but medical community stresses that there is no "benign melanoma" and recommends avoiding the term "malignant melanoma". Melanomas are usually caused by DNA damage resulting from exposure to UV radiation from the sun, but there are other risk factors for this cancer. Fortunately, people's awareness of this dangerous cancer is growing. More and more people understand the harm of overexposure to UV radiation during excessive exposure to sunlight and using indoor tanning facilities. In Poland, the use of tanning beds has been banned for people under the age of 18. There is also a complete ban on advertising and promoting the use of indoor tanning devices. In some countries, for example Brasil and Australia, there are laws prohibiting the use of indoor tanning facilities. Increasingly, people are effectively protecting themselves by applying sunscreen and avoiding the sun in the afternoon. Just as important as effective UV protection is regular skin checking. Early detection of melanoma offers the chance of a complete cure. This review includes risk factors, prevention and early detection of melanoma and highlights the importance of early detection of melanoma and ways to protect against it. The review also includes a study showing that simple text messages can increase people's knowledge about sun protection and skin self-examination.

## **Melanoma risk factors**

### **1. Exposure to ultraviolet radiation (UVR)**

Ultraviolet A (UVA) and ultraviolet B (UVB) radiation in sunlight and indoor tanning devices are the most indeed cause of skin cancer. Melanoma is caused by the malignant transformation of melanocytes, the cells that contain pigment [1, 2]. UVA radiation produces DNA strand breaks and reactive oxygen species, which can lead to DNA damage. Lower doses of UVB damage DNA, even though UVB is present in smaller amounts than UVA. Exposure to ultraviolet radiation (UVR) varies according to geographical location and latitude [3]

### **2. Low pigmentation**

Pigment production in the skin is induced by the melanocortin 1 receptor (MC1R). The MC1R is a cell surface receptor found on melanocytes. Many MC1R gene polymorphisms determine different skin phenotypes. The red hair and fair skin phenotype is associated with decreased pigmentation levels, making the skin more sensitive to UV radiation and ultimately increasing the likelihood of developing melanoma [4,5]

### **3. Age of sunburn and increased exposure**

There is an increased risk of melanoma in people exposed to high levels of UV radiation during childhood and adolescence [7]. People who had more than 5 episodes of severe sunburn are twice as likely to develop melanoma [8].

### **4. Comorbidities**

Patients with weakened immune systems, those who have undergone organ transplants, and individuals with a history of melanoma or other skin cancer are at a higher risk of developing melanoma compared to individuals with normal immune function [5, 6].

### **5. Genetic factors**

A family history [12] of melanoma is a strong risk factor for the disease. Individuals with atypical familial multiple moles and melanoma syndrome (FAMMM) or dysplastic nevus syndrome (DNS) have multiple, phenotypically variable moles. These moles are characterized by a high risk of malignant transformation, which creates a guaranteed lifetime risk of melanoma. Many people have numerous nevi, often due to cumulative sun exposure, without meeting the diagnostic criteria for these syndromes. Observational studies suggest that there is a strong association between a high number of nevi and melanoma. Patients with a family history of melanoma, dysplastic nevus syndromes and those with a large number of nevi should be kept under constant dermatological surveillance [15, 16, 17]. These patients should have a full-body dermatoscopic examination once every six months or quarterly [5].

### **6. Obesity [9]**

Obesity is associated with a significant number of metabolic and endocrine disorders. Some studies show that melanoma incidence may be associated with obesity. Obese people have increased levels of the growth factors insulin, IGF-1 and leptin in their blood. Adipocytes release lipids, chemokines, inflammatory factors and adipokines including leptin. all of them could impact on melanoma progression.

Clinical data suggest that leptin has been found to increase the proliferation of melanoma cells and the growth of the tumor. Many receptors are expressed on melanoma cells, including receptors for insulin and IGF-1, which correlate with melanoma progression [10, 11].

### Prevention of melanoma

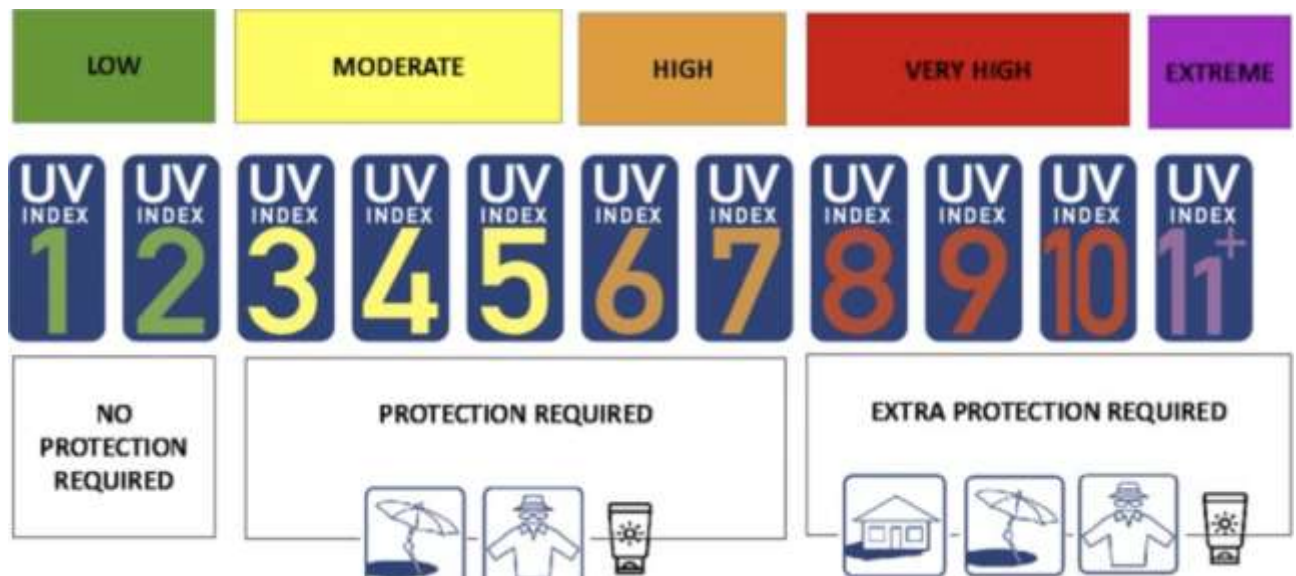


Image 1 UV Index-dependent recommendation of photoprotection [21,22 adapted by WHO]

The UV index, on a scale of 1 to 11, measures the intensity of solar UV radiation reaching the Earth's surface. It is provided by meteorological services and is available through different apps [14, 20]. The first pillar of UV protection is avoidance of UV exposure. This applies to sunlight and tanning beds. In some countries, there are laws prohibiting the use of indoor tanning facilities. The second pillar of protection is covering the body with clothing. Covering the body with clothing reduces the risk of sunburn. Many factors, such as the material and its density and colour, affect the protective properties of a clothing item [12]. It is recommended to use clothing with high UV Protection Factor. The third pillar of UV protection is the use of high protection sunscreens on exposed skin [22]

If the predicted UV index is 3 or higher, broad spectrum sunscreens are recommended. This applies to all exposed parts of the body [12, 13]. The scalp and ears should also not be forgotten. Ideally, applying sunscreen to the offset parts of the body should become part of the morning routine. The sunscreen should be reapplied every 2h, or even more frequently, especially after swimming, wiping the body with a towel [23].

Infants younger than six months should avoid direct sunlight. Employers should take steps to protect outdoor workers from UV exposure, such as adjusting work hours, providing breaks, shade, protective clothing, and sunscreen [12,14]

### Can text-messages help enhance prevention of melanoma? [25]

A randomized, attention control trial: „The Healthy Text” was carried out in 2012 and 2013 in Australia. The study was conducted to test the effectiveness of a behavioral intervention in the form of text messages in promoting sun protection and skin self-examination compared to attention control. The study included 546 participants aged between 18 and 42 years, who were randomly allocated to a group receiving text messages about:

Group 1: information on skin self-examination (176 people),

Group 2: information on sun protection (187 people),

Group 3: attention control (183 people).

The intervention groups received 21 text messages over a 12-month period. Information was gathered through phone surveys conducted at the beginning, 3 months in, and 12 months in Queensland from January 2012 to August 2013. One year into the study, it was found that those in the groups who received sun protection and skin self-examination information showed significantly greater improvement in sun protection habits compared to the attention control group. The increase in the proportion of participants reporting any skin self-examination from baseline to 12 months was significantly greater in the skin self-examination intervention group (103/163; 63%;  $P < 0.001$ ) than in the sun protection (83/173; 48%) or attention control (65/165; 36%) groups. [25] The conclusion of the Healthy Text intervention successfully improved sun protection and any type of skin self-examination behaviors.

### Early detection

Early detection of melanoma is very important. It offers the best chance of a complete cure. The prognosis for patients with melanoma depends only on the vertical depth of invasion. The risk of metastasis is very low in a thin melanoma lesion. The cancer must be detectable in its primary tissue at a stage when it can be easily treated.

### Skin self-examinations (SSEs)

#### Simple mnemonic device known as the “ABCDE Method” [26]

<i>Letter</i>	<i>Characteristic</i>
<b>A</b>	<b>Asymmetry</b> —benign moles typically have symmetric or uniform shapes, while cancerous moles are often asymmetric or irregular.
<b>B</b>	<b>Border</b> —benign moles have round and distinct borders, whereas cancerous moles often have asymmetric or jagged borders.
<b>C</b>	<b>Color</b> —benign moles tend to be a single color, while cancerous moles are often composed of multiple shades or colors at different parts of the mole.
<b>D</b>	<b>Diameter</b> —cancerous moles are typically over six millimeters in diameter. This is approximately the diameter of a common pencil.
<b>E</b>	<b>Evolving</b> —Unlike benign moles, cancerous moles often change in size, shape, and color over time.

Table 1 The ABCDE Method description [27]

Patients can quickly spot any abnormalities or changes by regularly monitoring their skin and moles. This method is quick and does not require any special equipment. However, patients are not able to examine every part of their body in such detail and depth. Unfortunately, it has been found that melanomas detected using this method are often worse to treat because they're advanced. This may be the result of patient inexperience in melanoma detection. [26, 27]

### **Seven-Point Glasgow checklist (7PCL) [26, 28]**

This is a method of examining nevi similar to the ABCDE method. It is recommended by The National Institute for Health and Care Excellence, and it is used by many doctors, mainly in the United Kingdom [29, 30]. The 7CPL identifies seven key criteria for differentiating between benign and cancerous moles and suggests consultation with a specialist if a score of  $\geq 3$  is achieved [29]. This method is more sensitive than ABCDE method.

Table 2 Characteristic of the Seven-Point Glasgow checklist method (7PCL) [27]

<i>Characteristic</i>	<i>Weighted Score Value</i>
Change in the size of a lesion	2 points
Irregularity in the shape of a lesion	2 points
Irregularity in the color of a lesion	2 points
Inflammation in or around the lesion	1 point
Alteration in sensation of the lesion	1 point
The lesion is large in size, or has a diameter larger than seven millimeters	1 point
Oozing or crusting on or around the lesion	1 point

### **The Ugly Duckling method [27]**

This is another method useful in evaluating moles [26]. It assumes that most of the nevi present in one person are similar to each other. Therefore, in this method, it is important to compare nevi against each other and look for those that differ from others. This is the simplest method for self-monitoring of moles. However, this simplicity does not convey any additional features to be aware of and leaves additional scope for some populations to downplay cancer symptoms in order to delay seeking professional advice. Therefore, the ugly duckling method should not replace other methods of examining moles, it should only complement them [27].

### **Dermatoscopy**

The dermatoscope is an effective tool for visually observing suspicious features associated with melanoma. It is a special magnifying device that allows doctors to look precisely at the skin [31]. The dermatoscope can also be connected to cameras to take high-resolution images. This tool has been shown to be very effective in detecting melanoma in both dermatologists and general practitioners. The use of the dermatoscope has been shown to increase doctors' sensitivity for melanoma from 76% to 92% [32].

The Dermatoscope is a valuable diagnostic tool in the detection of melanoma and can help in the fast and accurate diagnosis of this skin disease.

### **Future of early detection of melanoma [33]**

Numerous smartphone apps for self-assessment of skin lesions have been developed over the past few decades. More than half of these apps provide users with self-monitoring features, including the ability to log, organize and track moles using the built-in camera on their mobile device. Some apps act as an intermediary, sending images to qualified experts who use submitted images to assess potential risks. Other apps autonomously categorize lesions as either high or low risk and provide guidance on whether a medical consultation may be required.

### **Conclusions**

Melanoma, a malignant tumor of the melanocytes, is the most aggressive and deadly skin cancer. The incidence of melanoma is steadily increasing. Knowledge of melanoma risk factors allows effective prevention of this the most dangerous skin cancer. Early detection of melanoma makes it possible to cure it completely, which is why awareness among the public about the harmfulness of UV radiation is so important. There are many ways for effective protection from UV radiation such as using sunscreen, covering body with clothing, avoiding the midday sun and avoiding indoor tanning devices. The combination of all increases the strength of protection and therefore reduces the risk of melanoma. In addition to effective UV protection, it is important to check the skin regularly. With regularity people are able to recognize changes in existing moles and also catch those that are new. Screening is recommended for everyone in particular those with risk factors for melanoma, such as a family or personal history of melanoma, congenital disease or a predisposing lifestyle or occupation. The clinical diagnosis of melanoma is based on dermatoscopy, where suspicious lesions are evaluated using appropriate diagnostic criteria. Suspicious moles are referred for excisional biopsy. A definitive diagnosis is made on the basis of histopathological examination. Only early detection of melanoma makes it possible to cure and it reduce the mortality rate from this cancer.

### **Author's contribution:**

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