**How to Cite**:
Albogamy, S. A., Alnemer, Maram J., Aljawad, Hussain M., Alanazi, A. S. K., Alharbi, Abdulalah T., Al-Harbi, M. S. A., & Algfari, S. M. (2023). Melanoma: Risk factors, early detection, and treatment strategies-An updated review. *International Journal of Health Sciences*, *7*(S1), 3570–3588.
https://sciencescholar.us/journal/index.php/ijhs/article/view/15239

# Melanoma: Risk factors, early detection, and treatment strategies-An updated review

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***Abstract*---Background:** Melanoma is a significant and aggressive form of skin cancer originating from melanocytes. The rising incidence of melanoma, particularly among younger populations, underscores the need for increased awareness and early detection. **Aim:** This review aims to provide a comprehensive overview of the risk factors, early detection methods, and treatment strategies for melanoma, emphasizing recent advancements in the field. **Methods:** The review synthesizes current literature regarding melanoma's epidemiology, etiology, clinical presentation, diagnostic techniques, and therapeutic approaches. Emphasis is placed on advancements in immunotherapy, targeted therapies, and emerging nanotechnology-based strategies. **Results:** The global incidence of melanoma is increasing, with environmental factors such as UV radiation being the primary modifiable risk factor. Innovative treatment options, including

International Journal of Health Sciences E-ISSN 2550-696X © 2023.
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*Manuscript submitted: 01 Jan 2023, Manuscript revised: 09 Jan 2023, Accepted for publication: 15 Jan 2023*

immune checkpoint inhibitors and small-molecule kinase inhibitors, have shown promising results, although challenges such as drug resistance and adverse side effects remain. Recent clinical trials indicate that combination therapies may enhance treatment efficacy. Nanotechnology has emerged as a valuable tool for improving drug delivery and targeting tumor sites effectively. **Conclusion:** Melanoma poses a serious public health challenge due to its aggressive nature and rising incidence. Early detection through routine skin examinations and awareness of risk factors is crucial for improving outcomes. Continued research into novel treatment modalities, particularly utilizing nanotechnology, holds promise for enhancing the management of melanoma.

***Keywords*---**Melanoma, skin cancer, early detection, treatment strategies, nanotechnology.

## Introduction

The skin constitutes the largest organ in the human body, encompassing approximately 2 $m^2$ of surface area and weighing around 3.6 kg in adulthood. It serves crucial functions that ensure protection against physical, chemical, and biological threats, as well as regulating body temperature and synthesizing antimicrobial substances to avert infections [1,2]. The skin is stratified into three primary layers: the epidermis, primarily composed of keratinocytes (95%) along with various dendritic cells including melanocytes, Merkel cells, and Langerhans cells; the dermis, which consists of connective tissue, predominantly collagen and elastic fibers, alongside blood vessels, nerve endings, and glands such as sebaceous and sweat glands; and the hypodermis, which facilitates the connection between the dermis and the underlying organs [3,4].

Dermatological disorders impact millions globally, encompassing a broad spectrum of conditions ranging from chronic illnesses like atopic dermatitis and psoriasis to neoplastic diseases. While some of these are potentially treatable, the latter is linked to a high mortality rate [5,6,7]. Concerning skin cancers, the International Agency for Research on Cancer (IARC) reported approximately 1.52 million new cases and 121,000 related fatalities in 2020 [8,9]. A person succumbs to skin cancer every four minutes [10]. Furthermore, projections for the next two decades from the same agency are grim, anticipating increases of 78% and 73% in melanoma incidence and mortality, respectively [8,9]. Neoplastic transformations can arise in various layers of the skin, particularly within the epidermis. Malignancies of epidermal cells are classified into melanoma, which will be the focus of this study, and non-melanoma skin cancers, based on whether the originating cells are melanocytes or keratinocytes and Merkel cells, respectively [11,12].

The term "melanoma" is derived from the Greek words *melas*, meaning “dark,” and *oma*, meaning “tumor,” with its initial description credited to Hippocrates in the 5th century BC [13]. This aggressive condition originates from the malignant alteration and unchecked proliferation of melanocytes [14,15]. Melanocytes arise from a specific structure within vertebrate embryos known as the neural crest, and their primary role is to produce melanin (melanogenesis) and store it until it is transferred to keratinocytes [16,17,18]. Melanin serves as a vital pigment responsible for the coloration of the skin, hair, and eyes, playing a critical role in shielding the skin from ultraviolet radiation, neutralizing reactive oxygen species (ROS), and sequestering ions [19]. As previously mentioned, melanocytes predominantly inhabit the epidermis, specifically in the innermost layer known as the stratum basale [20]. The malignant transformation of these epidermal melanocytes leads to cutaneous melanoma, regardless of its metastatic status.

Cutaneous melanoma is the primary focus of this review, accounting for the vast majority of diagnosed cases [21,22]. Its major subtypes include superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, and acral lentiginous melanoma. Additionally, melanocytes can be found in other tissues, such as hair follicle bulbs, eyes, inner ears, mucosa, and the central nervous system, resulting in non-cutaneous forms of melanoma [21,22,23,24]. Notably, although melanoma is the least prevalent type of skin cancer, it remains the most aggressive and deadly [15,25,26]. Beyond its significant social implications, the high costs and complexities of advanced healthcare have garnered attention. For instance, in the United States, melanoma-related expenses account for approximately 40% of the annual budget allocated to skin cancer [14]. In contrast, despite a significantly higher incidence (18–20 times more), non-melanoma skin cancers, primarily Basal Cell Carcinoma (BCC) and Squamous Cell Carcinoma (SCC), exhibit slow growth and a low tendency to metastasize, making them rarely fatal [27,28,29,30].

In terms of therapeutic approaches, the management of melanoma has advanced significantly in recent years. Prior to 2011, available treatment options were mainly confined to surgery, radiotherapy, and chemotherapy [31,32]. The approval of the first immune checkpoint inhibitor, ipilimumab, and the first small-molecule kinase inhibitor, vemurafenib, marked a pivotal shift in treatment options. However, despite these substantial advancements, therapeutic limitations persist in certain cases, particularly concerning resistance and adverse side effects [32,33]. Consequently, alternative treatment strategies are continually being explored, whether in clinical or preclinical stages [34,35,36,37,38].

Nanotechnology, a concept introduced in the mid-20th century, has emerged as a valuable and promising tool [39]. Numerous lipid-based, polymeric, metallic, and hybrid nanosystems have already received approval for application in various fields, including oncology [40,41,42]. Enhancements in the physicochemical properties of compounds, such as increased water solubility and stability, coupled with improved pharmacokinetic and pharmacodynamic profiles, alongside the potential for targeted delivery of these nanosystems to tumor sites—either passively or actively—could revolutionize current therapeutic strategies for melanoma [43,44]. This review aims to present a comprehensive overview of the multifaceted aspects of cutaneous melanoma, encompassing its epidemiology, etiology, clinical presentation, prevention, diagnosis, staging, available conventional treatments, and the latest advancements in clinical trials involving new drug combinations, along with innovative nanotechnological approaches.

## Cutaneous Melanoma

### Epidemiology and Etiology

Melanoma is a form of malignancy whose global incidence has escalated significantly over the past few decades [14,45]. Populations with lighter skin, particularly in regions such as North America, Northern Europe, Australia, and New Zealand, have experienced an annual increase in melanoma incidence rates of 4–6% [14]. According to estimates by the International Agency for Research on Cancer (IARC), approximately 325,000 new cases of cutaneous melanoma were reported in 2020 [46]. Melanoma accounts for 1.7% of all cancer diagnoses [47], making it one of the most prevalent cancers worldwide, with an estimated 57,000 deaths occurring within the same timeframe [48]. Multiple factors contribute to this rising trend, including atmospheric ozone depletion, global warming, and air pollution [49,50]. The IARC has projected an increase of about 57% in new cases and 68% in related deaths by 2040 [51,52].

The process by which melanocytes transition into malignant cells is highly intricate, resulting from the interplay of various modifiable and non-modifiable risk factors [21]. Ultraviolet (UV) radiation exposure from sunlight or tanning devices is regarded as the primary modifiable risk factor for melanoma, accounting for approximately 60–70% of all diagnosed cases [53,54]. The IARC has classified these sources as carcinogens (Group 1), alongside tobacco and asbestos [55,56]. Consequently, it is unsurprising that the equatorial regions, characterized by extended sunlight exposure, report the highest melanoma incidence rates [22]. In 2020, the highest incidence rates of melanoma, as reported by the IARC, were observed in Australia and New Zealand, with age-standardized rates (ASR) per 100,000 individuals of 36.6 and 31.6, respectively. In contrast, countries with significant ASR were primarily situated at higher latitudes, including Denmark, The Netherlands, Norway, Sweden, Switzerland, and Germany [57]. Lower incidence rates have been noted in the southern regions of Europe, which can be attributed to differences in skin pigmentation among the populations, reflecting the patterns of incidence associated with ethnicity. The prevalence of darker skin pigmentation also accounts for the low ASR in other equatorial populations, such as many Asian and African nations [14,57]. Additionally, altitude has been suggested as a risk factor, as changes in ozone absorption, reduced cloud cover, and increased surface reflectance in snow-covered areas can elevate UV radiation exposure [14]. Approximately 6.8% of solar radiation is part of the UV spectrum, encompassing three types: UVC, UVB, and UVA (wavelength range: 200–280, 280–315, and 315–400 nm, respectively) [58]. UVC radiation, along with nearly all UVB radiation, is absorbed by the stratospheric ozone layer, allowing only 5% of UVB and 95% of UVA radiation to reach the Earth's surface [59,60]. Consequently, UVA and UVB radiation are primarily responsible for the mutagenic and proliferative effects on melanin-producing cells. UVB radiation not only causes direct DNA damage but also incites an inflammatory response that promotes angiogenesis and enhances the survival, proliferation, and metastatic potential of mutated cells. In contrast, UVA radiation induces DNA strand breaks, lipid peroxidation, and protein damage through oxidative stress [53,54,58,61].

While melanoma predominantly affects older individuals, there is a notable rise in prevalence among younger populations [14]. For instance, the average age at diagnosis for colon and lung cancers is 68 and 70 years, respectively, whereas melanoma is diagnosed at an average age of just 57 years [21,22]. Moreover, sex serves as a significant factor influencing melanoma incidence. In younger age groups, women exhibit a higher incidence rate, but this trend reverses with increasing age, leading to higher rates in men [21,22]. Despite this age-related shift, the overall incidence of melanoma remains greater in men than in women, with ASR of 3.8 and 3.0 per 100,000, respectively [47,63,64]. The reasons for this sex disparity remain incompletely understood; however, evidence suggests that both sex-specific behavioral factors and intrinsic biological differences play a role. For instance, female genetic heterogeneity, resulting from the epigenetic inactivation of one of the two X chromosomes, may contribute to this discrepancy [64].

The incidence of melanoma also varies significantly by ethnicity. Caucasians are more susceptible to melanoma compared to individuals with darker skin (2.4% vs. 0.1%) [45,65]. This differential risk is largely attributed to variations in skin color, influenced by factors such as carotenoid composition, oxy-/deoxy-hemoglobin levels, and, most notably, different types of melanin. Additionally, factors such as melanogenic activity, as well as the number, size, and packaging of melanosomes, impact skin color [60,66]. There are two primary forms of melanin present in the human body: eumelanin and pheomelanin. Eumelanin, a brownish-black pigment predominantly found in individuals with darker skin, offers protective benefits by dispersing and absorbing UV radiation and neutralizing free radicals. Conversely, the production mechanism of pheomelanin, a reddish-yellow pigment mainly synthesized in lighter-skinned individuals, can induce oxidative stress, leading to heightened susceptibility of melanocytes to DNA damage [60,67,68,69,70].

Lastly, given the substantial genetic component associated with melanoma, numerous genetic alterations (both hereditary and somatic) have been documented in recent years [71]. Germline mutations account for approximately 5–10% of cases, with the cyclin-dependent kinase inhibitor 2A (CDKN2A) mutation being the most prevalent. Additionally, mutations in several other genes, including melanocortin 1 receptor (MC1R), microphthalmia-associated transcription factor (MITF), cyclin-dependent kinase 4 (CDK4), protection of telomeres 1 (POT1), telomerase reverse transcriptase (TERT), adrenocortical dysplasia (ACD), telomeric repeat-binding factor 2-interacting protein 1 (TERF2IP), and BRCA1-Associated Protein 1 (BAP1), have also been identified in melanoma-prone families [72,73]. In contrast, somatic mutations are predominantly associated with the mitogen-activated protein kinase cascade, which can be categorized into four primary types based on the most frequently mutated genes: BRAF (serine/threonine protein kinase B-raf), the most prevalent, NRAS (neuroblastoma RAS viral oncogene homolog), NF1 (neurofibromin 1), and triple wild type (no mutation in any of these three genes) mutations [71,74,75]. Furthermore, certain genetic conditions, such as albinism and xeroderma pigmentosum, have been shown to heighten the risk of developing melanoma [76,77].

**Clinical Presentation**

Melanoma is recognized as one of the most diverse cancers, characterized by variations in both its causes and clinical features, influenced by factors such as its origin and anatomical site [79, 80]. There are four primary forms of cutaneous melanoma: superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, and acral lentiginous melanoma, each associated with distinct epidemiological, dermatological, and histopathological attributes [24, 81].

**Superficial Spreading Melanoma** accounts for 70-80% of melanoma cases and predominantly affects individuals aged 30 to 50 [82]. This type typically presents as a flat macule that may evolve into a palpable papule or nodule with irregular borders and a variety of colors. Histologically, it often shows a pagetoid and nested distribution of malignant melanocytes within the epidermis, along with intradermal nests of melanocytic proliferation [24, 83]. While it can develop anywhere, it is most commonly found on men's trunks and women's lower extremities. The horizontal growth phase can be prolonged before becoming invasive [82, 84].

**Nodular Melanoma** is the second most frequent type, representing 15-30% of cases. It can also arise in any location but is more prevalent on the trunk, head, and neck. This type of melanoma is the most aggressive [82]. Lesions can be brown, black, or even blue-black, presenting in various forms such as a polypoid exophytic tumor, an irregularly shaped plaque, or a smoothly surfaced cutaneous nodule. Histologically, it features intradermal nests and aggregates of tumor cells, with minimal intraepidermal melanocytic proliferation observed above the dermal tumor [83].

**Lentigo Maligna Melanoma** accounts for 5 to 15% of cases and is more common in older individuals with sun-damaged skin, particularly on the face, especially the nose and cheeks. This melanoma type is preceded by a skin lesion known as lentigo maligna, which may exhibit a horizontal growth phase lasting several years before it becomes invasive [82]. It typically appears as a flat tumor with tan, brown, and black irregular contours, featuring flecks of similar colors. Histologically, extensive melanocytic proliferation can be seen at the dermal-epidermal junction, extending through hair follicle epithelium, with intradermal nests of epithelioid or spindle-shaped cells [83].

**Acral Lentiginous Melanoma**, found in 2-8% of cases, predominantly affects people of color and typically develops on the palms of the hands and soles of the feet. It presents as an atypical pigmented macule that may progress to an elevated plaque or nodule [81, 82]. Histological features include extensive and poorly circumscribed lentiginous growth of nested tumor cells parallel to the epidermis [85]. Unfortunately, this variant is often diagnosed at more advanced stages [86]. Additionally, there are rarer variants of cutaneous melanoma, including desmoplastic, polypoid, primary dermal, verrucous, and amelanotic melanomas [24, 87].

**Prevention, Diagnosis, and Staging**

Addressing melanoma as a significant public health concern necessitates a focus on two key pillars: prevention and early diagnosis [45, 88]. Prevention efforts aim to enhance health literacy among the population, encouraging behavioral changes regarding modifiable risk factors and raising awareness about the importance of sun protection. Furthermore, there is increasing emphasis on closely monitoring individuals with high-risk characteristics for developing melanoma [54, 89, 90, 91].

Early and accurate diagnosis is crucial for improving outcomes, as five-year overall survival rates decrease from 99% when detected at stage IA melanoma to 15-20% in the most advanced stage (IV) [76]. Clinical diagnosis typically begins with the visual examination of suspicious lesions, supported by the ABCDE rule (Asymmetry, Border irregularity, Color heterogeneity, Diameter ≥6 mm, and Evolving) [92, 93]. For nodular melanoma, the mnemonic EFG (Elevated, Firm, and Growing) is utilized. A comparative dermoscopic analysis is also essential [26, 94]. Additionally, an excisional, punch, or shave biopsy should be performed whenever feasible, followed by histopathological examination. This analysis helps identify various parameters, including melanoma histotype, Breslow thickness, Clark level, mitotic index, and the presence or absence of ulceration [95, 96, 97].

Immunohistochemical analysis to identify melanocytic markers (such as S-100 protein, Melan-A, HMB-45, or SOX10), proliferation markers (MIB-1), lymph node biopsy, genetic characterization of targetable somatic mutations, and serum LDH level measurements may also be conducted in specific cases [26, 98, 99, 100]. Recent advancements have led to the development of numerous non-invasive pre-biopsy imaging technologies, including whole-body 3-D imaging, reflectance confocal microscopy, optical coherence tomography, high-frequency ultrasound, and multispectral digital skin lesion tools like MelaFind, which received FDA approval in 2011 [101, 102].

Accurate tumor staging is vital, allowing clinicians to evaluate patient prognosis and select the most suitable treatment strategy [103]. The American Joint Committee on Cancer (AJCC) employs the TNM staging system, which assesses three key aspects, each comprising multiple criteria: (T) Breslow tumor thickness of the primary tumor and presence or absence of ulceration; (N) number of affected lymph nodes and presence or absence of in-transit, satellite, and/or microsatellite metastasis; and (M) anatomic site of distant metastasis and LDH levels. Following analysis, patients are categorized into specific pathological stage groups, classified as stage 0, I (IA and IB), II (IIA, IIB, and IIC), III (IIIA, IIIB, IIIC, and IIID), and IV. In stage 0, cancer cells are confined to the epidermis, while stages I and II are classified based on tumor thickness and ulceration degree. Stages III and IV classification occurs with lymphatic tissue involvement and dissemination to one or more vital organs, respectively [104].

**Challenges and Opportunities for Cutaneous Melanoma Treatment**

As previously mentioned, in the early stages of the disease, the prognosis might be positive, and the patient can be successfully treated surgically [105]. However, as the disease progresses, survival rates significantly decrease [76]. Until 2010, only radiotherapy and chemotherapy were considered alternatives to surgery [31, 100, 106]. Later on, the growing knowledge about the pathogenesis of the disease, the role of the immune system, and the greater capacity for genomic sequencing allowed the identification of new targets [106, 107, 108]. Thus, marketing authorization of different drugs and/or combinations has taken place [107, 108, 109]. However, intra- and intertumoral heterogeneity continues to overlap, limiting therapeutic success [107, 110, 111]. According to the ClinicalTrials.gov database, a large number of clinical trials have been carried out testing new therapeutic strategies, including those based on nanotechnology.

**Current Available Strategies**

The currently available strategies for the treatment of melanoma are surgery, radiotherapy, chemotherapy, immunotherapy, and targeted therapy. The selection of the most suitable therapeutic strategy depends not only on the anatomic location, stage, and genetic profile of the tumor but also on the age and general health status of the patient [32]. The different therapeutic alternatives will be discussed in the following sections.

**Surgery Resection**

Whenever possible, surgical removal with adequate margins is the first-line treatment of melanoma [105]. Although it is mainly applied in patients up to stage II melanoma, it is also often an option for stage III patients [114, 115] or even when the disease has already metastasized to other organs (stage IV) [116, 117, 118, 119, 120]. However, especially in some patients at stages II and patients at stages III and IV, surgery alone has limited curative potential. Thus, radiotherapy, chemotherapy, immunotherapy, or targeted therapy are often used as adjuvant treatments [116, 121, 122].

**Radiotherapy**

Melanoma is a relatively radioresistant tumor as it has the ability to effectively repair DNA damage caused by radiation [123]. Therefore, the choice of radiotherapy as a first-line treatment is applied for exceptional cases, for example, given the impossibility of performing surgery or as a complement to some situations where there is a high risk of recurrence. On the other hand, radiotherapy is widely used as a palliative treatment for metastatic melanoma (stage IV). New techniques such as stereotactic radiosurgery and stereotactic body radiotherapy have commonly been used in the treatment of brain, lung, or liver metastases. Compared with whole-brain radiotherapy in the case of treatment of brain metastases, promising results and less severe adverse side effects have been observed [116, 124, 125]. Nonetheless, the combination of radiotherapy with systemic therapeutic options is currently under study in some clinical trials (NCT02858869 and NCT04902040) [126].

## Chemotherapy

Although chemotherapy remains a therapeutic option for melanoma management, especially in palliative or relapsed situations, new therapeutic choices are preferred in metastatic advanced stages of the disease [127]. The main disadvantages associated with chemotherapy are the lack of specificity for tumor cells and consequent low drug accumulation at the tumor microenvironment. Thus, therapeutic benefits are limited, and the incidence of adverse side effects is prominent [43, 123, 127]. To the best of our knowledge, the DNA alkylating agent dacarbazine (DTIC) remains the only drug approved by both FDA and EMA [128]. Generally, in the various clinical trials conducted, the DTIC response rate was around 10 to 20%, with most responses being partial and not sustained over time. In addition, nausea, vomiting, and myelosuppression are the most common adverse side effects [127, 129]. In addition to DTIC, and despite not being officially approved, many other chemotherapeutic agents have been used off-label, namely, temozolomide (TMZ), nitrosoureas, paclitaxel, docetaxel, and cis/carboplatin [100, 128].

TMZ is a DTIC analog approved for glioblastoma but frequently used in metastatic melanoma [127]. A phase III clinical trial comprising 305 volunteers with advanced disease found similar efficacy between both drugs (13.5 vs. 12.1% objective response rate for TMZ and DTIC, respectively) [130]. Besides this optimistic result, the oral route of administration and the ability of TMZ to cross the blood–brain barrier, relevant in the case of brain metastases, are other advantages [127, 131, 132]. Like the previous ones, nitrosoureas, such as photomustine, carmustine, and lomustine, are alkylating agents, generally used in combination with other drugs [127]. The anticancer activity of these compounds is identical to the gold standard, DTIC. However, they present a much unfavorable toxicity profile [129]. In turn, taxanes, such as paclitaxel and docetaxel, and platinum compounds, namely, carboplatin and cisplatin, have also been clinically tested in the treatment of melanoma as monotherapy. However, because of their moderate anticancer activity, the combination of these and other therapeutic classes continues to be investigated [127, 129, 131].

## Conclusion

Melanoma remains a critical public health concern due to its increasing incidence and mortality rates. This review highlights the multifactorial nature of melanoma, where both genetic and environmental factors contribute significantly to its development. The role of UV radiation exposure as a primary modifiable risk factor is underscored, particularly in light-skinned populations, where the incidence continues to rise alarmingly. Education and awareness about sun protection and early detection strategies are essential in mitigating the risk and improving prognosis. The advancements in melanoma treatment have been substantial over the past decade, with the introduction of targeted therapies and immunotherapy representing significant milestones. Immune checkpoint inhibitors, such as ipilimumab and nivolumab, have revolutionized melanoma management, leading to improved survival rates in advanced stages of the disease. However, therapeutic challenges remain, including the emergence of drug resistance and the need for personalized treatment approaches based on individual genetic profiles. Emerging nanotechnologies present exciting possibilities for enhancing melanoma treatment. By improving drug solubility, stability, and bioavailability, nanocarriers can facilitate targeted delivery of therapeutic agents to tumor sites. This targeted approach not only increases the efficacy of treatments but also minimizes systemic side effects, which is particularly beneficial in managing advanced melanoma cases. In conclusion, while significant progress has been made in understanding and treating melanoma, ongoing research is vital. Future studies should focus on elucidating the molecular mechanisms underlying melanoma progression, refining early detection strategies, and exploring innovative therapeutic avenues, including nanotechnology. Collaborative efforts among researchers, clinicians, and public health officials will be essential to combat melanoma effectively and improve patient outcomes.

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**الميلانوما: عوامل الخطر، الكشف المبكر، واستراتيجيات العلاج - مراجعة محدثة.**

**الملخص:**

**خلفية :** الميلانوما هي شكل خطير وعدواني من سرطان الجلد ينشأ من الخلايا الميلانينية. إن الزيادة في حالات الميلانوما، وخاصة بين الفئات الشابة، تؤكد على الحاجة إلى زيادة الوعي والكشف المبكر.

**الهدف :** تهدف هذه المراجعة إلى تقديم نظرة شاملة على عوامل الخطر وطرق الكشف المبكر واستراتيجيات العلاج للميلانوما، مع التركيز على التقدمات الحديثة في هذا المجال.

**الطرق :** تجمع المراجعة الأدبيات الحالية المتعلقة بوبائية الميلانوما، وأسبابها، وعرضها السريري، وتقنيات التشخيص، والنهج العلاجية. يتم التركيز على التقدمات في العلاج المناعي، والعلاج المستهدف، والاستراتيجيات الناشئة القائمة على تكنولوجيا النانو.

**النتائج :** تزداد معدلات الميلانوما عالميًا، حيث تُعتبر العوامل البيئية مثل أشعة الشمس فوق البنفسجية هي العامل الرئيسي القابل للتعديل. أظهرت خيارات العلاج المبتكرة، بما في ذلك مثبطات نقاط التفتيش المناعية ومثبطات كيناز الجزيئات الصغيرة، نتائج واعدة، على الرغم من وجود تحديات مثل مقاومة الأدوية والآثار الجانبية السلبية. تشير التجارب السريرية الحديثة إلى أن العلاجات المركبة قد تعزز فعالية العلاج. لقد برزت تكنولوجيا النانو كأداة قيمة لتحسين توصيل الأدوية واستهداف مواقع الأورام بشكل فعال.

**الاستنتاج :** تشكل الميلانوما تحديًا خطيرًا للصحة العامة بسبب طبيعتها العدوانية وارتفاع معدلات حدوثها. يُعد الكشف المبكر من خلال الفحوصات الجلدية الروتينية وزيادة الوعي بعوامل الخطر أمرًا حاسمًا لتحسين النتائج. إن البحث المستمر في طرق العلاج الجديدة، لا سيما استخدام تكنولوجيا النانو، يحمل وعدًا بتحسين إدارة الميلانوما.

**الكلمات المفتاحية :** الميلانوما، سرطان الجلد، الكشف المبكر، استراتيجيات العلاج، تكنولوجيا النانو.