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THE IMPACT OF PHYSICAL ACTIVITY AND RELATED FACTORS ON THE RISK OF MELANOMA DEVELOPMENT AND PROGRESSION OF THE DISEASE - A LITERATURE REVIEW

Authors:

Joanna Szuba (JS)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0000-7880-7523
joanna.szuba.15@gmail.com

Magdalena Rędaszka (MR)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0003-0679-6732
magda.red22@gmail.com

Oliwia Barańska (OB)
Bielanski Hospital, 80 Ceglowska street, 01-809 Warsaw, Poland
https://orcid.org/0009-0008-5512-7048
oliwiafilomena@gmail.com

Małgorzata Chańko (MC)
Specialist Hospital Wejherow, 10 dr. A. Jagalskiego Street, 84-200 Wejherowo, Poland
https://orcid.org/0009-0009-4571-0763
malgorzata.chanko@gmail.com

Justyna Drożdżał (JD)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0008-1403-4777
justyna.drozdzal8@gmail.com

Adam Krzaczkowski (AK)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0005-5851-587X
adam.krzaczkowski@onet.pl

Emilia Niedzieska (EN)
Central Clinical Hospital, Medical University of Warsaw,
1a Banacha street, 02-097 Warsaw, Poland
https://orcid.org/0009-0004-8946-1344
emilia.niedzieska@gmail.com

Zofia Szular (ZS)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0000-8854-1116
zszular@gmail.com

Tymon Wojczulis (TW)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0002-0602-0427
t.wojczulis@gmail.com

Katarzyna Ziemek (KZ)
Infant Jesus Clinical Hospital, Medical University of Warsaw,
4 Lindleya street, 02-005 Warsaw, Poland
https://orcid.org/0009-0007-6947-0624
kasiaziemek@gmail.com

Abstract

Introduction

In 2020, around 325,000 new melanoma cases were diagnosed globally, with 57,000 resulting deaths. The highest incidence was observed in Australia and New Zealand, while much lower rates occurred in African and Asian countries. Melanoma was generally more common in males. The global rise in melanoma—possibly linked to increased travel and tanning device use—calls for identification of modifiable risk factors and predictors. Lifestyle elements, especially physical activity and body weight, play a major role in cancer risk and progression.

Purpose of research

This review aims to explore how physical activity and related factors affect melanoma risk and disease progression. It also examines sun-protection awareness, behaviors, and melanoma risk among outdoor athletes.

Materials and methods

In 2025, a literature review was conducted using PubMed, Web of Science, and Google Scholar, focusing on English-language studies analyzing the link between amateur or professional physical activity and melanoma. Search terms included "physical activity," "exercise," "athletes," "melanoma," and "photoprotection."

Summary

Numerous preclinical studies examine the influence of physical activity on the tumor microenvironment. Another key focus is the impact of exercise on melanoma patients undergoing immunotherapy. Epidemiological data emphasize sun exposure as a major risk factor, particularly for physically active individuals. Therefore, consistent use of sun protection is essential from an early age, especially for both professional and recreational athletes. Primary care physicians should conduct regular skin exams for active individuals, particularly swimmers. Future research should explore both behavioral and biological mechanisms and determine whether physical activity independently affects melanoma risk markers, such as telomere length and naevus count.

Keywords: melanoma, physical activity, exercise, skin cancer

Introduction and objective

Physical activity is a well-known protective factor against the risk of several types of cancer, with the most substantial evidence supporting its benefits for colon and breast cancer. With the global incidence of malignant melanoma on the rise potentially due to increased long-distance travel and the use of tanning devices it is crucial to identify modifiable risk factors and markers. Additionally, investigating whether physical activity can influence or predict the development of malignant melanoma is of significant importance [1].This review aims to evaluate the impact of physical activity and related factors on the risk of melanoma development and progression of the disease. The occurrence of melanoma in areas seldom exposed to UV radiation, along with the association between naevus patterns (location and number) and both the histology and site of melanoma, indicates the existence of distinct pathways leading to melanoma development [2], [3], [4]. In addition, several genetic factors have been linked to melanoma incidence, including naevus development, genes associated with pigmentation, melanin production, DNA repair, a family history of melanoma [5], [6], [7] and immunosuppressive therapy [1].
In 2020, an estimated 325,000 new melanoma cases were reported worldwide (174,000 in males and 151,000 in females), along with 57,000 deaths (32,000 males and 25,000 females) [8].The occurrence of both non-melanoma skin cancer and melanoma kept rising [9].
Significant geographic differences were observed across countries and world regions, with the highest melanoma incidence rates recorded in Australia/New Zealand—42 per 100,000 person-years for males and 31 per 100,000 person-years for females. Western Europe followed with 19 per 100,000 person-years for both sexes, while North America reported 18 per 100,000 for males and 14 per 100,000 for females. In Northern Europe, incidence rates were 17 per 100,000 for males and 18 per 100,000 for females. Melanoma remained uncommon in most African and Asian countries, where rates typically fell below 1 per 100,000 person-years. Mortality rates reached a peak of 5 per 100,000 person-years in New Zealand, though geographic disparities were less pronounced for mortality than for incidence. Across most world regions, melanoma was more prevalent in males than in females. If the rates from 2020 persist, the global melanoma burden is projected to rise to 510,000 new cases—a nearly 50% increase—and 96,000 deaths—a 68% increase—by 2040 [8].
Physical activity is believed to help prevent cancer by strengthening immune function, enhancing DNA repair capacity, reducing oxidative stress, lowering chronic inflammation, and maintaining a healthy weight [10], [11], [12], [13], [14]. However, research on the relationship between physical activity and melanoma risk has yielded mixed findings, with studies reporting positive, inverse, or no association [14]. Nevertheless, the connection between physical activity and cutaneous malignant melanoma (CMM) has not been thoroughly explored [15], [16]. The role of sunlight exposure, a recognized risk factor for cutaneous malignant melanoma (CMM) is inseparable connected with skin's exposure to UV radiation- a widely recognized risk factor for melanocyte transformation [14], [17]. A significant aspect of outdoor physical activity, has rarely been considered in studies examining this relationship [15], [16].
Lifestyle factors, including physical activity and body weight play a crucial role in influencing cancer risk and progression. Substantial evidence indicates that physical activity lowers, while obesity elevates, the risk and mortality associated with various cancer types. In non-obese individuals, energy restriction (ER) has been shown to significantly decrease tumor occurrence across multiple preclinical models and to reduce body weight along with cardiometabolic risk factors in humans. Emerging research suggests that the cancer-preventive effects of physical activity and ER may stem from their impact on inflammatory and immune mediators. Physical activity modifies the tumor's gene expression profile and immune infiltrates, potentially reducing immunosuppressive factors. However, morel studies are needed to confirm these findings [18].

Methods

We searched PubMed, Web of Science, and Google Scholar for English-language publications investigating the association between amateur and professional physical activity and melanoma (prevention, incidence, treatment). We primarily focused on articles published between 2014 and 2024, including review articles, animal studies, observational studies, and clinical trials. To identify relevant publications, we used the following keywords in various combinations: "physical activity," "exercise," "athletes," "melanoma," and "photoprotection." Articles were initially screened based on their titles and abstracts.

1. Animal model studies

Several studies have investigated the effects of exercise on tumor biology. In one experiment, Savage et al. compared the response to exercise in two phenotypically and genotypically distinct murine models of melanoma – B16F10 and YUMMER 1.7. They found that exercise inhibited tumor growth and increased $CD8^+$ T cell infiltration only in the YUMMER model, classified as an "exercise-responsive" tumor. Vascular remodeling was observed in both models; however, physical activity reduced hypoxia exclusively in YUMMER tumors. Both models showed increased expression of VCAM1 on the tumor endothelium in treadmill-exercised mice compared to sedentary controls. The authors concluded that exercise significantly increased MHCII gene expression and expanded antigen-presenting cell populations. Furthermore, the study identified a role for ERK5 S496 phosphorylation (an exercise-responsive residue) in regulating tumor vascular adhesion molecule expression and tumor-associated macrophage (TAM) polarization [19].

In an experiment by Hojman et al., using mice, it was confirmed that physical activity has a protective effect against cancer, regardless of BMI. Running significantly reduced melanoma growth in both chow-fed and high-fat-fed mice. A dose- and time-dependent effect of exercise on tumor growth was also observed. Furthermore, it was reported that ZBP1 (a cytosolic DNA-sensing molecule) may be associated with the regulation of exercise-dependent induction of innate immunity, as evidenced by its strong correlation with myeloid and NK cell markers in B16F10 tumors. However, no effect of ZBP1 was observed on exercise-regulated necrosis in the tumors of exercising mice [20].

In turn, the study by Dos Santos et al. showed the effect of moderate exercise on melanoma growth and tumor non-infiltrated lymphocyte function in obese mice. The study observed a significant reduction in melanoma growth in mice fed a high-fat diet and exposed to moderate exercise. Moreover, in this group of animals, increased proliferation of tumor non-infiltrated lymphocytes and decreased serum levels of leptin were noted. A significant reduction in the secretion of IL-2, IFN-γ, and TNF-α was also observed. It can be concluded that these changes contribute to the reduction of chronic inflammation that accompanies both obesity and the neoplastic process [21].

A preclinical study by Pedersen et al. presented that physical activity undertaken four weeks before tumor cell implantation reduced tumor growth by 61% [22]. In the experiment by Buss et al., it was found that short-term exercise training after melanoma implantation did not alter the rate of tumor growth, hypoxia, perfusion, blood vessel density, or cell proliferation. Only a physiological effect of exercise was noted, in the form of a significant increase in the heart to body weight ratio in exercising mice. This suggests that the use of exercise as a monotherapy after tumor cell inoculation has limited efficacy; therefore, further research is needed to explore the combination of physical exercise with other cancer treatment strategies [23].

In the study by Yan et al., significant inhibition of tumor growth and tumor cell proliferation was observed in a group of melanoma-bearing mice subjected to combined treatment with exercise and anti-PD-1 therapy. Following this combined intervention, a significant increase in IFN-γ, perforin, and granzyme B levels was reported in tumor tissues, along with a decrease in IL-10. The findings suggest that physical exercise enhanced tumor immunoinfiltration by mitigating intratumoral hypoxia [24].

Moreover, the study by Bay et al. found that among three murine tumor models (melanoma B16F10 cells, breast cancer E0771 cells, and Lewis lung carcinoma (LLC) cells), the B16F10 melanoma model was the most responsive to physical activity, measured as voluntary wheel running, in terms of immune checkpoint molecule expression (PD-1, PD-L1, PD-L2, CD28, B7.1, and B7.2). However, the study also observed that combining physical activity with immune checkpoint blockade therapy did not result in an additive effect [25].

In an exploratory study conducted by Buss et al., the effects of tumor presence and anti-PD-1 immunotherapy on the mitochondrial response of skeletal muscle to exercise training were investigated in murine models of B16-F10 melanoma and EO771 breast cancer. In the melanoma model treated with anti-PD-1 antibodies, exercise training elicited an increase in the majority of assessed markers of mitochondrial content within skeletal muscle. Conversely, administration of the isotype control antibody (IgG2a) did not induce similar mitochondrial adaptations. In the EO771 breast cancer model, exercise led to an increase in most mitochondrial markers regardless of whether the mice received anti-PD-1 or IgG2a treatment. These findings suggest that the interaction between tumor type, immunotherapy, and physical activity may differentially influence skeletal muscle mitochondrial adaptations, and underscore the potential of exercise interventions in mitigating cancer-related muscle wasting during immunotherapy [26].

Furthermore, the study by Lee et al. revealed that exercise, in the B16F10 melanoma model, promotes enhanced pro-apoptotic signaling, shifts ceramide metabolism toward a pro-apoptotic ceramide/sphingosine-1-phosphate balance, and leads to increased tumor cell death. However, the same intervention in the BP melanoma model did not result in the accumulation of pro-apoptotic ceramides, which may indicate a differential impact of physical exercise depending on the melanoma model [27].

2. Results of bioinformatics analyses

The results of bioinformatic analyses contribute to a better understanding of the molecular mechanisms underlying the effects of physical exercise on melanoma [28], [29]. In an integrated bioinformatics analysis conducted by Zhu et al., pivotal exercise-induced genes in malignant melanoma were identified. The study revealed a total of 1,627 differentially expressed genes—1,285 with increased expression and 342 with decreased expression following exercise. The exercise-related genes in melanoma were associated, among other things, with the modulation of self-defense mechanisms and immune system processes. The top six hub genes identified were Itgb2, Wdfy4, Itgam, Cybb, Mmp2, and Parp14. Notably, melanoma patients with high expression levels of Wdfy4, Parp14, Cybb, Itgb2, and Itgam demonstrated longer overall survival. These findings suggest a potential prognostic value of exercise-induced genes and provide a foundation for further in-depth studies [28]. Meanwhile, a bioinformatics analysis by Xia et al. identified 294 upregulated genes and 21 downregulated genes in the exercise group. Additionally, the study showed 10 candidate hub genes, including C3, Kng1, C3ar1, Ptafr, Fgg, Alb, Pf4, Orm1, Aldh3b1, and Apob. In particular, the genes C3, C3ar1, Kng1, Ptafr, and Fgg may play critical roles in the complement and coagulation cascade pathway and the *Staphylococcus aureus* infection pathway [29].

3. Physical activity and melanoma: studies involving humans

3.1. Patients with melanoma at various stages of advancement

The advantages of exercise for individuals with cancer are now undeniable. Engaging in physical activity both during and after treatment has been proven to improve their well-being and overall quality of life [30]. The human studies we found mainly focused on patients with advanced melanoma and/or those undergoing immunotherapy [31], [32], [33]. However there is a limited number of studies on advanced skin malignancies such as melanoma. Hyatt et al. demonstrated that 27% of melanoma patients usually participate in physical exercise but abstain from it during immunotherapy [31].

The i-Move pilot trial evaluated the safety, adherence to, and acceptability of a personalised exercise programme in 30 patients with stage IV melanoma who were scheduled to receive, or had recently received immunotherapy. In addition, the aim of this study was to provide evidence of the efficacy of exercise in combating immunotherapy-related fatigue. The randomised controlled trial has been completed but the results are not yet available.

A 12-week personalised exercise programme, delivered via a smartphone app, was tailored to each participant, taking into account physical, health, and social aspects. It included moderate-intensity aerobic exercise, resistance training, and stretching of major muscle groups. An exercise physiologist was responsible for designing the exercises, monitoring progress, and consulting with the patients [32].

Similarly, the Sportivumab study (NCT03171064) investigated the feasibility of exercise as an adjunct therapy in patients with melanoma treated with immune checkpoint inhibitors. Patients in the experimental group engaged in machine-based endurance and resistance training twice weekly for 12 weeks, guided by an exercise therapist. Secondary outcome measures included physical activity behaviour, cardiopulmonary fitness, muscle strength, and quality of life. The results of this study have not yet been published [33].

The role of physical activity in people with unresectable stage III/IV melanoma was explored in a study by Hyatt et al. Australian participants of a cross-sectional survey were either currently receiving immunotherapy or had recently completed treatment. Fifty-six percent of patients reported engaging in physical activity during immunotherapy, with 35% exercising twice per week and 26% three times per week. Walking was the most commonly chosen activity (77%), while pilates and group sports were the least common. Light physical exertion lasting up to 30 minutes, such as gardening and swimming, was also frequently reported. The most commonly perceived benefit of physical activity was reduced fatigue; however, fatigue itself was also the most frequently reported barrier to participation [31].

Interesingly, outcomes were noted in the retrospective analysis by Carmeli and Bartoletti, highlighting a statistically significant relationship between elevated levels of physical activity and improved quality of life in both localized and regional melanoma survivor [34]. In contrast, the study by Lacey et al. found no alterations in quality of life in patients with regional and metastatic melanoma after 8 weeks of multimodal supportive care [35].

3.2. Melanoma survivors

An increasing amount of research has shown that physical activity enhances various aspects of cancer survivorship. Multiple randomized trials investigating the impact of physical activity on cancer survivorship across different cancer types have shown that participants in exercise groups experienced significant enhancements in overall quality of life, physical function [36], mental well-being [37], reduced distress [38], and improved sleep [38]. These findings reinforce the message that, even for individuals who were inactive before their cancer diagnosis, adopting physical activity afterward may help mitigate cancer-related complications in melanoma survivors [36], [37], [38], [39].

Even long-term melanoma survivors with early-stage disease may face adverse physical and psychological effects, such as persistent distress and enduring physical symptoms [40], [41], [42].

Among the participants, 724 melanoma survivors (62%) and 660 control individuals (60%) completed the follow-up survey, though 21 respondents did not fill out the physical activity section. Overall, melanoma survivors and the control group shared similar demographic and health characteristics, except for differences in skin tone and smoking habits. Additionally, melanoma survivors reported spending fewer hours outdoors during peak sun exposure (10 AM – 4 PM) compared to controls (1.7 hours vs. 2.1 hours, $P < 0.0001$) [43].

Unfortunately, some melanoma survivors stop exercising or reduce their level of physical activity. This is demonstrated by an observational study by Robinson, which compared the physical activity of melanoma survivors (stage 0-1A) pre-diagnosis, and at 2-3 months and 12 months after surgical treatment. Before diagnosis, all study participants were physically active; however, following surgery, approximately one-third of women were inactive (30% at 2–3 months and 31% at 12 months). The study showed that inactivity at 12 months post-surgery was positively correlated with older age and female sex. Among younger participants (aged 27–40 years), moderate-mild physical activity was most common at 2–3 months post-treatment (62%), while vigorous activity predominated at 12 months (75%) [44]. In a large population-based study by Bøhn et al., the lifestyles of 246 young adult melanoma survivors (≥ 5 years post-diagnosis) were analyzed. Up to 45% of survivors were physically inactive, and 53% had a BMI ≥ 25. This study indicated that chronic fatigue remained associated with physical inactivity [45]. Adequate sun protection among melanoma survivors is also a critical concern. In an observational study by Robinson et al., UV and physical activity sensors were used to calculate the protection-adjusted UV dose. Melanoma survivors exceeded the minimal erythema dose (MED) for the forearms or lower legs during outdoor activities ($P < 0.001$). Sunburn was reported by 45% of participants on at least one body area. The occurrence of sunburn was significantly associated with spring temperatures in the Midwest of the United States and walking activity. While sun protection was commonly used on the face, the forearms and lower legs were often insufficiently protected during outdoor walking. In contrast, melanoma survivors who engaged in outdoor water sports employed more effective sun protection measures and did not report sunburn [46].

3.3. Fatigue and physical activity in patients with melanoma

The outlook for melanoma has been transformed in recent years due to advancements in immunotherapy and targeted treatment. However it is also connected with the many implications that affect the patient's quality of life [30]. Declines in quality of life are frequently observed due to treatment-related toxicities and tend to be more severe in patients with regional or metastatic disease [47], [48], [49], [50]. Fatigue is a common side effect reported by patients undergoing immunotherapy and affects all areas of daily life. Patients often lack knowledge of effective methods to help reduce its severity [51]. In a prospective study of German patients with metastatic melanoma, who were scheduled to receive immune checkpoint inhibitors, side effects and stress levels were assessed. Fatigue was the most common side effect reported by patients, regardless of the treatment regimen (monotherapy – 32.5% or combination immunotherapy – 29.7%) [52]. Research has shown that exercise and psychological support effectively alleviate cancer-related fatigue both during and after treatment, significantly outperforming available pharmaceutical options [30], [50].

3.4. Physical activity as an aspect of supportive care

In recent years, scientific research has increasingly focused on the concept of supportive care for oncology patients. Previous studies have indicated the positive impact of supportive care interventions on patients' coping abilities, disease-related knowledge, and adjustment to the diagnosis. Physical activity is a key component of this model of care, alongside psychoeducational elements [53].

Boileau et al. conducted a pilot study to assess the feasibility of a prospective investigation into changes in quality of life three months after initiating an adapted physical activity (APA) programme in patients with melanoma. In addition, the study evaluated physical activity levels and barriers to participation in the program among 271 patients diagnosed with melanoma, 75% of whom were at stage IV, and 81% of whom were receiving immunotherapy. A total of 61.31% of participants reported walking or cycling for at least 10 minutes each way, while 16.50% engaged in high-intensity physical activity. The most frequently reported barrier to APA participation was transport-related issues, such as distance to the hospital (31.88%). Notably, all participants had a consultation with an exercise physiologist, during which their physical activity level was assessed and personalised exercise recommendations were provided [54].

Furthermore, the cross-sectional survey by Thompson et al. identified supportive care needs of Australian patients diagnosed with melanoma and their caregivers. Patients with advanced-stage melanoma reported significantly more unmet psychological and physical needs. This group also presented significantly poorer functioning across all functional scales and experienced greater fatigue compared to patients with early-stage disease. A small percentage of early-stage melanoma patients had access to (2%) or expressed a desire to access (14%) an exercise physiologist. In contrast, among patients with advanced disease, these figures were notably higher—approximately 28% wished to consult an exercise physiologist, and 25% expressed interest in seeing a nutritionist [55].

The widespread use of telemedicine techniques in oncological care became particularly prominent during the SARS-CoV-2 pandemic [56]. One interesting and promising aspect of telemedicine is the delivery and supervision of physical activity in patients. In a pilot study, Crosby et al. assessed the feasibility, safety, and preliminary efficacy of an exercise program (aerobic, resistance and balance activities) supervised via telehealth. Participants had been diagnosed with stage III/IV melanoma and were receiving checkpoint inhibitor therapy. The authors reported significant improvements in physiological outcomes, such as cardiovascular capacity and upper body strength. However, no change in body weight was observed. This innovative exercise program was initially found to enhance physical fitness while maintaining quality of life, without serious adverse events. It may also provide an opportunity for further research aimed at improving existing programmes [57].

4. Physical exercise and risk of cancer

Beyond regulating energy balance and affecting body composition and BMI, exercise may have a direct impact on the tumor microenvironment. Physical activity enhances the structure and functionality of blood vessels. Tumor vasculature is often abnormal due to disruptions in the balance of pro- and anti-angiogenic signals within a growing tumor, leading to dysfunctional blood vessels characterized by dilation, excessive branching, and permeability [58]. Inefficient vasculature results in tumor hypoxia, which subsequently increases tumor aggressiveness, facilitates metastasis, and reduces the effectiveness of chemotherapy, targeted therapy, and radiotherapy [58], [59], [60], [61], [62], [63]. Additionally, hypoxia is a critical factor in the malignant transformation of melanocytes.
A recent study suggested that the observed positive association between bone mineral density and naevus count (and, consequently, melanoma incidence) might be partially attributed to leucocyte telomere length. However, whether this relationship is causal remains uncertain, as the study did not account for sun exposure as a potential confounder, and leucocyte telomere length has been inversely linked to sun exposure, naevus count, and melanoma incidence [64], [65]. It remains unclear whether physical activity influences leucocyte telomere length and naevus count [66], [67], [68]. A sizable cross-sectional study found a positive correlation between physical activity and naevus count in 26,000 men, but not in 67,000 women after adjusting for age [68]. The noted gender disparity might be explained by confounding from sun exposure, as women are less prone to engage in outdoor physical activities compared to men, and when they do, they tend to have lower serum vitamin D levels than men in each outdoor physical activity group [69]. Perier et al.'s study found that seasonal physical activity was not linked to melanoma risk. There were positive correlations between overall physical activity and sunbathing vacations as well as indoor tanning, and, contrary to existing literature, an inverse relationship between overall physical activity and sunburns [70].

5. Melanoma exposure in proffesional and recreational athletes and their sun exposure habits

In health research, the most commonly used assessment is cardiorespiratory fitness (CRF), which indicates how effectively the circulatory and respiratory systems deliver oxygen during prolonged physical exertion. Consequently, CRF serves as an objective marker of sustained aerobic exercise over time, though it does not account for all forms of physical activity [71]. The relationship between melanoma skin cancer and physical activity appears to trend in the opposite direction, though without statistical significance [71], [72]. Further analysis based on the anatomical location of the melanoma indicated that the risk increase was observed only for the head and trunk [71]. Moreover, studies relying on self-reported physical activity indicate a positive association with skin cancer [17]. This may be because physically active individuals tend to spend more time outdoors than inactive individuals, leading to higher exposure to UV radiation from the sun, the primary risk factor for skin cancer [14], [17], [73].

5.1. Aquatic sports

Some studies have shown that athletes who participate in outdoor sports are exposed to higher levels of UV radiation and, consequently, have an increased risk of developing skin cancer [74]. Most of the available research pertains to aquatic athletes. A pooled sample of 4,377 participants from six countries participating in five water-based sports were analyzed, revealing that basal cell carcinoma (BCC) (71%) was the most prevalent skin cancer, followed by melanoma (18%) and squamous cell carcinoma (SCC) (10%). However, the main finding is that individuals involved in water-based sports face a significant risk of developing skin cancer, especially on the upper body, which is related to the challenges in maintaining sun protective behaviours [75]. One of the most favored outdoor water activities in Australia is surfing, with around 2.7 million leisure surfers estimated; nonetheless, Australia has long been acknowledged for having the highest rate of melanoma globally, and this is the most prevalent form of cancer among young Australians. A total of 1,348 surfers, with 56.9% being recreational, took part in this study. Among them, 184 surfers reported having skin cancer, including 96 competitive and 87 recreational surfers. Regarding non-melanoma and melanoma cases, basal cell carcinoma (BCC) was the most frequently reported (6.8%), followed by melanoma (1.4%) and squamous cell carcinoma (SCC) (0.6%). The relative risk was significantly higher ($P < 0.001$) in competitive surfers compared to recreational ones [OR 1.74 (CI 1.28–2.31)]. Skin cancers were most commonly reported on the face (23.5%), back (16.4%), and arms (12.4%). Notable trends were observed in skin cancer cases between competitive and recreational surfers. Additionally, men (14.6%) reported significantly more skin cancers than women (9.4%) [76].

5.2. Educational campaigns for athletes

It is still necessary to promote awareness and educate athletes about the importance of sun protection. For example, in 2019, the Clever in Sun and Shade Program (CSSP) was established to highlight the benefits of UV protection among sports school students [77]. The study conducted by Ally et al. represents a compelling example of an effective educational intervention—SUNSPORT—targeted at student-athletes, athletic trainers, and coaches within the National Collegiate Athletic Association (NCAA). Post-intervention analyses showed an increase in the proportion of individuals reporting sunscreen use on four or more days per week, rising from 26% to 39%. Furthermore, the proportion of student-athletes who reported receiving sun safety recommendations from their coaches more than doubled, from 26% prior to the intervention to 57% following its implementation ($P < 0.0001$). Additionally, the intervention was associated with a notable shift in risk perception, with 67% of participants acknowledging that athletes constitute a high-risk group for skin cancer, compared to 54% prior to the intervention. [78].

5.3. Athletes' knowledge and practices regarding sun protection

A survey conducted by Weikert et al. assessed golfers' interest in various sun protection strategies. Alarmingly, 39% of respondents did not believe that playing golf increased their risk of skin cancer. Golfers who had experienced a golf-related sunburn in the past year showed greater interest in a wider range of interventions, including educational resources, family support, and text message reminders [79]. In a separate survey by McCarthy et al. involving Irish golfers, awareness of skin cancer risk factors and sun protection behaviours was evaluated. A previous diagnosis of melanoma was reported by 4.9% of participants. Additionally, 72% of respondents acknowledged an increased risk associated with sunburn or sun exposure. While 85% of participants reported using sunscreen during play, nearly half (44%) used a product with a sun protection factor (SPF) below the recommended threshold of 30 [80]. In comparison, only 23.3% of American golfers reported frequent sunscreen use. Furthermore, 36% of athletes consistently used sunscreen while playing golf and expressed interest in interventions such as sunscreen dispensers and UV forecast boards on the course [79]. Awareness of the risks associated with UV radiation exposure does not always translate into the adoption of appropriate photoprotective behaviours among athletes (Table 1.). A study of elite kitesurfers revealed their attitudes towards sun exposure. Although most athletes reported being afraid of developing skin cancer due to sun exposure (79.2%), a large proportion admitted that they enjoyed sunbathing (44.4%) or felt that sunbathing improved their well-being (45.8%). Worryingly, 31.9% of respondents stated that they disliked using sunscreen [81]. Comparable attitudes were identified in the study by Gutiérrez-Manzanedo et al., in which the vast majority of outdoor rock climbers (88.9%) were aware that ultraviolet radiation could cause various forms of skin cancer. Despite this high level of awareness, 63.6% also reported enjoying sunbathing, and 71.3% indicated that they did not like using sunscreen [82].

5.4. Skin examinations among athletes

An important element of melanoma prevention among athletes is both self-examination and specialist examination of moles conducted by a dermatologist. There remains a need to expand public awareness campaigns on this subject. Evidence suggests that, regardless of age, athletes rarely perform self-examinations for suspicious skin lesions [83]. Skin examinations of Croatian triathletes revealed that 46% had solar lentigines and 25% presented with atypical naevi. Additionally, 26% of respondents reported a history of severe sunburns accompanied by blistering [84]. In a study by De Castro-Maqueda et al. concluded that 83.3% of outdoor sports practitioners (including elite surfers, windsurfers, and Olympic sailors) had not undergone dermatological examination, while 87.5% reported performing self-examinations for moles and skin lesions. Despite prolonged UV exposure—70.9% spent between one and four hours in the water daily, and 29.1% exceeded four hours—a concerning 22.5% of participants never used sunscreen, and 31.1% failed to reapply it after two hours [85]. In an observational study based on online surveys conducted by Doncel Molinero, 14 Spanish cyclists (1.43%) reported having been diagnosed with melanoma. The study also found that younger cyclists (under 40 years of age), those exposed to the sun for at least three hours per week, and individuals who rarely or never used sunscreen were more likely to experience sunburn. Moreover, although 3.4% of respondents reported a personal history of skin cancer, 61% did not regularly examine their skin [86]. In a cross-sectional study by Miller et al., during a screening of 423 athletes, a dermatologist identified 167 participants (39.5%) with actinic keratosis, 253 participants (59.8%) with keratinocyte carcinoma, and 22 participants (5.2%) with malignant melanoma. Surfers were twice as likely to have malignant melanoma compared to swimmers (6.48% vs. 3.33%) and one and a half times more likely compared to walkers/runners (6.48% vs. 4.3%) [87].

5.5. Sun safety awareness and photoprotection during outdoor physical activity in children and adults

Adherence to physical activity guidelines should be encouraged across all population groups and increasingly promoted. However, engaging in outdoor physical activity entails additional exposure to UV radiation and therefore necessitates appropriate photoprotection. The risk of sunburn is heightened during physical exertion conducted in outdoor environments [88]. A study by Dona et al. investigated the relationship between adherence to physical activity guidelines (≥150 minutes of moderate-to-vigorous or ≥75 minutes of vigorous physical activity per week) and sun-related health behaviours. Among participants meeting the physical activity recommendations, 56.8% of those residing in rural areas and 46.9% from urban areas reported experiencing at least one sunburn in the previous year. The study found no other significant differences in reported sun protection behaviours based on physical activity status, regardless of residential setting. Interestingly, urban residents who met physical activity recommendations were less likely to seek shade, whereas this association was not statistically significant among rural participants. Notably, only a small proportion (28.5%) of individuals meeting physical activity guidelines reported using sunscreen [89]. Outdoor physical activity should be encouraged from an early age. Parents and teachers play a crucial role in modelling healthy behaviours; however, they do not always adhere to recommended sun protection practices [90], [91], [92]. In a descriptive cross-sectional study by Blázquez-Sánchez et al., both children (<11 years) and adolescents (11–17 years) demonstrated high levels of sun exposure during outdoor sports and recreational activities. Inter-group comparison analysis revealed that children adhered more closely to photoprotective recommendations than adolescents [93]. A study by Wu et al. compared outdoor physical activity among parents and children living in urban and rural areas. During sports, the incidence of sunburn was higher among rural parents than their urban counterparts. Women were more likely than men to experience sunburn while engaging in sports. Additionally, boys were more prone than girls to sunburn on days when they exercised. Parents reported that their daughters were more likely to reapply sunscreen and to tan intentionally outdoors than their sons. The use of sunscreen and seeking shade during outdoor activities were more common among urban parents than those living in rural areas. A higher proportion of urban children also reported frequent sunscreen use—either through self-report or parental report—compared with rural children. Therefore, tailored interventions for melanoma prevention should consider the specific needs of both rural and urban families [90].

5.6. Sun protection attitudes among physical education teachers

There are also studies examining attitudes towards sun exposure among physical education (PE) teachers, who are expected to serve as role models for their students [90], [91]. However, their behaviours do not always reflect recommended sun safety practices. This group is particularly vulnerable to sunburn and its associated health risks. A cross-sectional study conducted by Barón et al. included Spanish PE teachers working in primary and secondary public schools. On average, they spent 2.7 hours outdoors per day, with many outdoor activities occurring during periods of peak UV index. Using personal dosimetry, the study found that PE teachers were exposed to solar radiation doses two to three times higher than the levels recommended by international health authorities. Among the reported photoprotective behaviours, the most common were wearing sunglasses (84%) and using sunscreen (79.6%), while seeking shade was the least frequently practised (16%) [91]. Another study involving Spanish teachers compared the sun protection habits of PE teachers (n = 100) and teachers of other subjects (n = 100). Consistent with previous findings, PE teachers experienced greater sun exposure than their counterparts. Statistically significant differences ($P < 0.01$) were observed in weekday sun exposure, with the highest proportion of PE teachers (34%) spending 120 minutes in the sun on weekdays. The study also revealed gender-based differences in sunscreen use within both groups, with men reporting less frequent use than women. Notably, 44% of PE teachers reported no sunburn episodes in the preceding 12 months. However, 91% of all participants had never conducted a skin self-examination. Furthermore, among PE teachers, 88% of men and 93% of women stated they had never undergone a dermatological examination [92].

Table 1. Summary of research on sun protection behaviours among athletes.

STUDY	GROUP OF ATHLETES (n)	USE OF SUNSCREEN WITH SPF (often–always)	ATHLETES WITHOUT HISTORY OF SUNBURN (%)	REGULAR SELF-SKIN EXAMINATION (%)	FEAR OF GETTING SKIN CANCER FROM SUN EXPOSURE (%)	ATHLETES WHO LIKE TANNED SKIN (%)
Gutiérrez-Manzanedo et al. [82], 2023	outdoor rock climbers (n=217)	49.3	34.1	-	84.2	51.7
Doncel Molinero et al. [86], 2022	cyclist (n=1018)	39.2	54.4	39.0	94.9	41.8
Tenforde et al. [94], 2022	runners (n=697)	42.0 (on face) 18.0 (on the body)	-	-	39.2	6.1
Castro-Maqueda et al. [85], 2020	surfers (n=79)	91.0 (m)[1] 92.0 (w)[2]	22.0 (m) 21.0 (w)	9.0 (m) 21.0 (w)	-	-
Castro-Maqueda et al. [85], 2020	windsurfers (n=48)	89.0 (m) 83.0 (w)	14.0 (m) 17.0 (w)	17.0 (m) 33.0 (w)	-	-
Castro-Maqueda et al. [85], 2020	Olympic sailors (n=113)	82.0 (m) 94.0 (w)	3.0 (m) 21.0 (w)	2.0 (m) 17.0 (w)	-	-
Castro-Maqueda et al. [81], 2020	elite kitesurfers (n=72)	79.2	15.3	21.2	79.2	52.8
Castro-Maqueda et al. [83], 2019	beach hand ball players: 1. university students (n=73)	53.4	26.0	5.5	-	-
	beach hand ball players: 2. younger players (n=48)	58.4	18.8	12.5	-	-
Fernández-Morano et al. [95], 2017	skaters	18.7	43.1	-	-	-

1) men, 2) women

Table 2. Three distinct relationships between physical activity and melanoma risk.

1. Positive association
A combined evaluation of longitudinal studies and a systematic review identified significant links between physical activity and the likelihood of melanoma [16], [17], [71], [72]. A significant issue in the cohort study was the potential distortion caused by risk factors associated with ultraviolet (UV) radiation [72]. The primary risk factor for melanoma is skin damage caused by UV radiation, encompassing a history of sunburns, the presence of dysplastic and common nevi, actinic keratosis, and solar lentigines [72], [96], [97], [98], [99]. Among the additional factors increasing the risk of melanoma are those that heighten vulnerability to skin damage caused by UV radiation, including complexion type, hair and eye shade, presence of freckles, tanning capacity, and the skin's initial response to sun exposure at the start of the tanning period [72], [98].
2. No association
However there are studies which shows no significant association between life-course physical activity and melanoma risk [14], [70], [100], [101]. In Perrier's et.al study participants provided information on their current physical activity level at recruitment, alongside their past physical activity levels at ages 14 and 30. They used a validated 10-point scale, which was accompanied by the following clarification: "By physical activity we mean activity both at work and outside work, at home, as well as training/exercise and other physical activity, such as walking, etc. Please mark the number that best describes your level of physical activity;being very low and 10 being very high." In response to this question, physical activity refers to the total amount of physical activity across various domains—recreational, occupational, transport-related, and domestic chores [14].
3. Negative association
Interestingly, melanoma risk showed a positive correlation with serum leptin levels and a negative association with healthy lifestyle factors. However, these findings require validation in future prospective studies [102]. Moreover, Shors et.al observed that engaging in physical activity on most days of the week (five to seven) was associated with a lower melanoma risk in both males and females [100].

6. Anthropometric measure

Excess body weight is recognized as a well-documented risk factor for 13 distinct types of cancer [103]. Biologically active, adipocytes produce cytokines, estrogens, and adipokines. Imbalances in adipokines, such as leptin and adiponectin, can either stimulate or suppress the growth of various cancers [104], [105]. Adiposity also causes systemic metabolic disturbances, including metabolic syndrome and elevated blood levels of insulin and IGF-1, which can activate oncogenic signaling pathways like the PI3K pathway [106], [107]. Recent studies have suggested that the adipokine leptin directly promotes melanoma growth by binding to leptin receptors on tumor cells [108], [109] and increasing risk of sentinel lymph node metastases [110]. Leptin levels in humans have also been associated with an increased risk of melanoma [111]. It should be emphasised that direct interaction between adipocytes and melanoma cells has been identified, with the transfer of lipids from adipocytes promoting melanoma tumor development in preclinical models [112].

Body mass index (BMI) has been inconsistently identified as a risk factor for melanoma. A higher melanoma risk was noted among men in the upper quartiles of height (OR = 2.4, 95% CI = 1.3-4.5), weight (OR = 2.8, CI = 1.5-5.2), and body surface area (OR = 2.8, CI = 1.5-5.1) compared to those in the lowest quartiles. Conversely, no significant association was observed between melanoma risk and any anthropometric parameter in women. Furthermore, the analysis demonstrated that individuals of both genders who engaged in physical activity five to seven times per week had a reduced probability of developing melanoma. However, the underlying mechanisms explaining the role of physical activity and the gender differences in anthropometric influences remain uncertain [100].

Obesity is linked to a poorer prognosis in early-stage melanoma but it was connected to markedly better outcomes in patients with metastatic melanoma undergoing treatment with BRAF-targeted therapy or immune checkpoint

inhibitors. Men may derive greater benefits from obesity than female. Possible mechanisms include the influence of sex hormones on tumor and immune cells, as well as the immunosuppressive effects of leptin on T cells, which may unexpectedly enhance responsiveness to anti-PD1 therapy. However, it remains uncertain how the "obesity paradox" could be leveraged to improve treatment outcomes [113].
These are the potential explanations:
Frequently, the survival benefit is confined to the overweight category (BMI 25–29.9), where excess weight may be misidentified as it could be attributed to growth of muscle mass instead of fat accumulation [114]. Nonetheless, in melanoma, a dose-dependent effect was noted, with the likelihood of progression or mortality diminishing as BMI increased, extending into severe obesity [115]. Other possible reasons for an obesity-related survival benefit include reverse causality, where patients with more aggressive disease experience prior weight loss and a shift to a lower BMI category, while the obese may have increased "met abolic reserves" to endure the debilitating effects of cancer or its treatment [116], [117]. Most notably, the survival benefit of obesity in melanoma was particularly observed in immune and targeted therapies, which generally do not induce weight loss, while no BMI-related association was found in chemotherapy groups [118]. Notably, an interplay was detected between biological sex and BMI, where the obesity-related benefit was exclusive to males. Being female is a well-recognized positive prognostic factor in melanoma [119], [120].

7. Vitamin D

It is widely recognized that sunlight, particularly ultraviolet B (UVB) rays, is essential for the effective production of vitamin D [121]. The primary defense mechanisms that safeguard human skin from UV radiation include melanin production and active DNA repair processes. DNA is the main target of both direct and indirect UV-induced cellular damage. Insufficient pigmentation, particularly in individuals of Caucasian descent, along with rare congenital defects in DNA repair, are key factors contributing to protection failures. Nucleotide excision repair (NER) is a crucial mechanism that helps prevent skin cancer by repairing UV-induced DNA damage. Its significance is evident in the rare genetic disorder *xeroderma pigmentosum* (XP), where mutations in various NER genes result in extreme sensitivity to UV radiation and a heightened risk of skin cancer.A growing collection of findings suggests that nucleotide excision repair (NER) is not the sole DNA restoration mechanism implicated in UV-triggered melanoma and nonmelanoma skin cancer formation. A novel viewpoint in the study of DNA damage and repair emerges from the involvement of mammalian mismatch repair (MMR) in rectifying UV-induced genetic alterations. The MMR enzyme hMSH2, which acts as a p53-regulated gene, is activated by UVB exposure and participates in NER pathways. Consequently, research efforts have been launched to clarify the biological and pathological significance of MMR in the progression of malignant melanoma and nonmelanoma skin cancers. UVB, and to a much lesser extent UVA, can cause molecular DNA alterations that lead to the formation of specific photoproducts, which are recognized as mutagenic. The genotoxic effects of UVA are mainly attributed to oxidative damage to DNA [122].

Moreover vitamin D impact extends well beyond the regulation of calcium and phosphorus balance, as various functions of vitamin D and its natural metabolites ensure the proper functioning of key human organs, including the skin [121].The primary source of vitamin D is the exposure of the epidermis to sunlight. In a photochemical reaction, 7-dehydrocholesterol (7-DHC) is converted into vitamin D3 under UVB light (280–320 nm) in the keratinocytes of the basal layer of the epidermis [121]. Once released into the extracellular space, vitamin D is absorbed in the capillary network by vitamin D binding protein (DBP) [123]. Vitamin D synthesized in the skin or acquired through diet is biologically inactive and must undergo two hydroxylation processes to become fully hormonally active [123], [124]. Initially, vitamin D3 is transformed into 25-hydroxyvitamin D3 (25(OH)D3) within hepatocytes by the essential enzyme vitamin D 25-hydroxylase, known as CYP2R1 [125], [126]. 25(OH)D3 is the main metabolite of vitamin D, and its serum level is commonly used in clinical settings to assess vitamin D status [124].

Recent research has also indicated that occupational exposure to solar radiation may actually act as a melanoma protective factor [127]. However, it is also important to consider that past occurrences of sunburns significantly rais the likelihood of melanoma. It must be emphasized that optimal skin production of vitamin D does not necessitate prolonged sunbathing. As little as roughly 15 minutes of exposure of the arms and legs on a sunny day (0.25–0.50 minimal erythemal dose (MED) is adequate to produce the equivalent of about 2,000–4,000 IU of vitamin D [128].
Moreover, it appears that new vitamin D analogues with minimal or no effect on calcium levels are promising candidates not only for topical therapy but also for broader use in the prevention and treatment of various skin or systemic human conditions [121]. It seems that vitamin D plays a crucial, physiologically significant role in preventing UV-induced carcinogenesis [122]. Several recent studies have highlighted that the development of melanoma may be associated with vitamin D deficiency or disruptions in the vitamin D signaling pathway [129],

[130], [131]. Due to its antiproliferative characteristics, vitamin D and its analogues are promising candidates for melanoma therapy. In fact, it has been demonstrated that the metabolites of vitamin D suppress cell proliferation and stimulate the differentiation of melanoma cells expressing VDR [132], [133], [134]. Interestingly, it appears that normal melanocytes and keratinocytes are protected by 1,25(OH)2D3 and its analogues [135]. There is a proof that $1\alpha,25(OH)_2D_3$ enhances cell viability while suppressing tumor progression and blood vessel formation [136], [137]. The VDR gene exhibits multiple splicing variants in the human body, which are likely to influence protein expression and VDR activity. Furthermore, more than 1,000 polymorphic sites have been identified in the VDR gene, some of which have been linked with an elevated risk of melanoma development, its severity, and prognosis [138].

Vitamin D can influence immune responses by enhancing the innate immune system while suppressing the adaptive immune response. It reduces chronic inflammation associated with an increased risk of cancer [139], [140]. Vitamin D affects the inflammatory immune response by upregulating PD-1, as seen in Crohn's disease[141], and stimulates the production of programmed death-ligand 1 (PD-L1) and PD-L2 through VDR in experimental cell models [142]. The regulation of the immune response by vitamin D is associated with the suppression of type 1 T-helper (Th1) cells and the enhancement of the Th2 phenotype, including the increased expression of interleukin 10 (IL-10) and TGF-β [143], [144].
The onset, progression, disease-free and overall survival of melanoma patients may be associated with disruptions in vitamin D signaling. Altered local vitamin D levels could result from changes in vitamin D metabolism within melanoma cells. The anti-melanoma effectiveness of vitamin D depends on the proper functioning of both VDR and the metabolizing enzymes. As VDR, CYP27B1, CYP24A, and ROR expression are associated with melanoma patient prognosis, they may serve as potential biomarkers [145].

Conclusions

This epidemiological analysis indicates that melanoma continues to be a significant obstacle to cancer prevention and public health worldwide, particularly among fair-skinned individuals of European origin. Melanoma association was stronger in high UV areas, implying that sun exposure is an important factor underlying this association. Based on findings in these all studies there is no doubt that physically active individuals should consistently implement sun protection measures, such as avoiding peak ultraviolet radiation hours (10 AM–3 PM), wearing a rash vest and hat, and applying sunscreen. Additionally, primary care physicians should routinely screen their patients who participate in exercise especially in surfing. It is important to raise awareness about effective sun protection among both recreational and professional athletes. Future research in basic and epidemiologic science should focus on biochemical or behavioral explanations for these observations. Well-designed future studies are needed to investigate whether physical activity independently influences leucocyte telomere length, naevus count, and melanoma incidence, apart from sun exposure. Consequently, exercise is recommended to decrease the fatigue that patients experience as a result of their immunotherapy treatment.

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