# The Effect of Sunscreen on Melanoma Risk

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**KEYWORDS**

• Cutaneous melanoma • Melanoma risk reduction • Sunscreen • UV protection • SPF

**KEY POINTS**

- While the etiology of melanoma is multifactorial, individuals who are exposed to intense sunlight intermittently are at highest risk for developing melanoma.
- Intermittent exposure to ultraviolet radiation is the only known modifiable cause of melanoma, but the role of sunscreen in preventing melanoma remains somewhat controversial.
- Evidence suggesting a positive association between sunscreen application and melanoma risk reduction is growing.
- Recent studies suggest that the regular use of sunscreen can prevent the development of melanoma by up to 10 years.

## INTRODUCTION

Exposure to UV radiation is a known risk factor for the development of melanoma and nonmelanoma skin cancers.[1] Over time, sun exposure is known to cause DNA damage and systemic immunosuppression, which are factors for carcinogenesis.[2–4] Total cumulative sun exposure is associated with the development of squamous cell and basal cell cancers, whereas intense intermittent sun exposure has been associated with the development of melanoma.[5,6]

A history of sunburn in particular seems to be an important risk factor for the development of melanoma.[7] The results of a meta-analysis conducted by Dennis and colleagues[8] showed that sunburn carries a lifetime relative risk for melanoma of up to 1.6 across all age groups. In addition, the relationship between UV exposure and melanoma risk was found to be dose dependent. An increasing number of lifetime sunburns was associated with a linear increase in the risk of melanoma. It should be noted, however, that a history of sunburns might simply be a proxy for a strong history of recreational sun exposure because individuals who are infrequently exposed to UV radiation are more likely to burn when exposed to sunlight intermittently.

The cause of melanoma is multifactorial. In addition to genetic predisposition, phenotypic characteristics, such as fair skin, red hair, freckling, and proclivity to sunburn, all contribute to melanoma risk as does living in sunny locations or at high altitudes. Although exposure to UV radiation is the only known modifiable cause of melanoma, the role of sunscreen in melanoma prevention remains somewhat controversial.

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## UV RADIATION AND THE PATHOGENESIS OF MELANOMA

UV light is classified according to its physical properties, namely wavelength. UV-A light occurs in the 320- to 400-nm wavelengths, UV-B light in 290- to 320-nm wavelengths, and UV-C light in 100- to 290-nm wavelengths. UV-C radiation is filtered by the ozone layer, whereas UV-A and UV-B radiation reach the earth's surface and have been strongly implicated in the development of cutaneous melanomas.[9,10]

UV-A radiation is far more abundant in natural sunlight than UV-B radiation. The primary mechanism through which UV-A radiation injures cells is through the formation of free radical species. By causing oxidative DNA damage, UV-A light acts as a potential mutagen.[11] UV-A radiation is also thought to have substantial immunosuppressive effects. Exposure to UV-A radiation in mice has been shown to prevent the local immunologic rejection of certain skin cancers.[12] In other studies, UV-A radiation has been shown to induce the development of melanomas in opossums and in certain fish.[13,14]

Although only 5% to 10% of the UV radiation that reaches the earth's surface falls in the UV-B spectrum, UV-B radiation is the major contributor to sunburn and is responsible for causing DNA damage. UV-B penetrates to the basal layer of the epidermis where it leads to the formation of pyrimidine (thymine) dimers in DNA.[15–18] The incorrect repair of these DNA lesions can lead to mutations that alter cell function.[11,16,18] The role of UV-B in the development of cutaneous melanoma has been demonstrated in melanoma-susceptible transgenic mice.[19]

Individuals who are exposed to intense sunlight intermittently are at the highest risk for developing melanoma. Melanoma is most common in persons with indoor occupations whose primary exposure to UV radiation is recreational, such as on weekends and vacations. This pattern of sun exposure in melanoma is further evidenced by the fact that melanoma tends to develop in areas of the body that are primarily subject to intermittent UV radiation. For example, men are typically affected on the back, whereas women are typically affected on the lower legs. In contrast to squamous cell and basal cell cancers, melanoma typically spares the face, hands, and forearms.

## SUNSCREENS

### *Mechanism*

UV light is a known carcinogen and, therefore, it is important to protect against the harmful effects of UV-A and UV-B radiation. Sunscreens are agents that temporarily block UV radiation absorption by the skin. Lotions, creams, protective clothing, umbrellas, sunglasses, and hats all qualify as sunscreen agents. Topically applied sunscreen agents are categorized as either organic or inorganic UV filters. Organic filters absorb UV radiation, whereas inorganic filters scatter and reflect UV radiation. There are advantages and disadvantages to both types of formulations. Most commercially available sunscreens contain a combination of organic and inorganic filters.

Inorganic UV filters, such as zinc oxide and titanium dioxide, were previously known as physical sunscreens. When photons of UV radiation contact submicroscopic sunscreen particles, they are dispersed in various directions. These agents do not break down over time and are generally well tolerated. Their major drawback is cosmetic; inorganic filters do not blend into the skin as easily as organic preparations and can result in a whitish discoloration of the skin.

Organic UV filters, previously known as chemical sunscreens, function by absorbing photons of UV radiation. These agents are highly effective and are typically more easily applied than inorganic agents because they are in the form of creams and lotions. Unlike inorganic agents, they tend to degrade with sun exposure and require frequent reapplication. In addition, organic sunscreens have the potential to penetrate the skin, resulting in systemic exposure.[20,21] Finally, organic agents may cause a variety of adverse skin reactions, including allergic contact dermatitis, photoallergic dermatitis, irritant dermatitis, acne, and other aesthetic issues.[22] These reactions occur infrequently, but the prominence of organic UV filters as allergens is increasing because of the increased use of soluble UV filters in daily face moisturizers.

### *The Sun Protection Factor System*

The efficacy of a sunscreen should ideally be measured by the extent to which the sunscreen protects from skin cancer, but because these studies are difficult to perform, surrogate endpoints are used. The sun protection factor (SPF) system measures the ratio of time it takes to sunburn with sunscreen protection divided by the time it takes to burn without protection.[23] When determining the SPF, a sunscreen application thickness of 2 mg/cm$^2$ is used. Because UV-B radiation causes sunburn, the SPF of a sunscreen measures protection from UV-B radiation only. For example, an SPF of 15 filters 94% of UV-B and an SPF of 30 filters 97% of UV-B. As SPF increases to more than