CONSENSUS STATEMENT

Expert Consensus on Sunscreen for the Primary Prevention of Skin Cancer: Results from the Skin Cancer Prevention Working Group Conference

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ABSTRACT

Background: Melanoma and non-melanoma skin cancers (NMSC) are the overall most common type of malignancy. Despite this fact, the use of sunscreen as a primary preventative measure for skin cancer is not ubiquitous.

Objective: To review the literature regarding efficacy and safety of sunscreens and to process and condense data into overarching principles to provide guidance to the public and improve outcomes for melanoma NMSC.

Methods: A systematic review of the literature pertaining to sunscreen efficacy in the primary prevention of melanoma and non-melanoma skin cancer, safety in humans and environmental impact was conducted. Following a thorough review of the literature, the Skin Cancer Prevention Working Group (SCPWG), an expert panel consisting of dermatologists with specialized training in melanoma and NMSC diagnosis and management, employed a modified Delphi technique to reach consensus over the development of statements regarding the current level of evidence for sunscreen efficacy and safety. Final statements were only adopted after achieving a supermajority vote >80%.

Results: 96 articles were identified for further review and discussion. The SCPWG developed 7 consensus statements regarding the efficacy and safety of sunscreens and their role in the prevention of melanoma and NMSC.

Conclusion: The proven benefits of primary skin cancer prevention outweigh the potential/hypothetical risks of sunscreen use, especially given insufficient real-world, prospective data for the discussed risks. As experts in skin health and skin cancer pathophysiology, the SCPWG believes dermatologists are uniquely qualified to lead future studies investigating sunscreen efficacy and safety and should counsel patients and the public on skin cancer primary prevention strategies.
Skin cancer (including melanoma and non-melanoma skin cancer (NMSC)) accounts for the greatest incidence of new cancers in the US, with upwards of 200,000 cases of melanoma (~50% of which are invasive) and ~5.4 million cases of NMSC diagnosed annually.\textsuperscript{1-6} Diagnosis and management of skin cancer accounts for $6 billion in yearly US healthcare expenditures.\textsuperscript{7} Early diagnosis and treatment, especially for melanoma, is critical to improve patient outcomes.\textsuperscript{8,9} However, despite significant improvement in understanding of cancer pathophysiology, diagnostic armament, and treatment efficacy and modalities, over 7000 individuals in the US die from advanced melanoma annually.\textsuperscript{3,10} For this reason, one of the best forms of skin cancer management is primary prevention.

One of the primary drivers of skin cancer is exposure to ultraviolet radiation (UVR).\textsuperscript{11} Studies attribute 90% of melanomas to deleterious UVR-induced genetic mutations, primarily from UVA radiation (320-400 nm wavelength) and UVB (280-320 nm).\textsuperscript{11} Known methods to reduce harmful UVR exposure include decreasing time in direct sunlight, seeking shade, wearing dark-colored clothing, and regularly applying (and re-applying) sunscreen.\textsuperscript{12,13}

The active ingredients in sunscreen are typically composed of mineral-based inorganic agents (e.g. Zinc Oxide (ZnO), Titanium Dioxide(TiO\textsubscript{2})) or organic compounds (e.g. oxybenzone, avobenzone, octinoxate, octisalate, homosalate, octocrylene).\textsuperscript{14} Combinations of these filters are capable of broad-spectrum protection against UVA and UVB.\textsuperscript{15} Despite data showing the ability of these agents to reduce UVR-induced erythema and decrease long-term incidence of melanoma and NMSC, questions have arisen regarding hypothetical systemic and environmental harms of sunscreen use, including concerns that misinformation may cause unwarranted harms to patients.\textsuperscript{16-24}

The purpose of this expert consensus panel was to synthesize the most current available literature regarding sunscreen efficacy and safety into overarching principles, providing a framework with which dermatologists, physicians, and other non-physician providers may better counsel patients.

**METHODS**

**Literature Search**

A systematic review of the literature pertaining to the sunscreen efficacy in the primary prevention of melanoma and non-melanoma skin cancer and safety regarding human use and environmental impact was conducted. The MEDLINE database was queried for all relevant articles using exploded MeSH terms and keywords pertaining to the themes of efficacy (incidence, mortality, primary prevention, skin cancer, melanoma, non-melanoma skin cancer, basal cell carcinoma, cutaneous squamous cell carcinoma) and safety (organic sunscreen, mineral sunscreen, oxybenzone, avobenzone, octinoxate, octisalate, homosalate, octocrylene, titanium dioxide, zinc oxide, environment, patient education, and systemic absorption). The Boolean term “AND” was used to find the intersection of these themes with the term “sunscreen.” 96 articles were deemed relevant to the discussion of sunscreen safety and efficacy based on full-text review were selected for further review and analysis by members of the consensus panel.
Consensus Development Process
A 7-person consensus panel of dermatologists representing the Skin Cancer Prevention Working Group (SCPWG), physicians with specialized training in the diagnosis and management of melanoma and non-melanoma skin cancer, convened during May 2021. Panel members discussed issues regarding the efficacy of sunscreen in skin cancer prevention and potential systemic and environmental effects given the current findings and data in the literature. Statements were drafted based on review and analysis of the selected articles and relevant discussion.

Consensus among panel members was achieved using a modified Delphi technique, which has previously been used in developing dermatologic expert panel recommendations to reach consensus.25-27 For consensus, a supermajority (>80%) agreement among participants was required. If a statement did not obtain supermajority approval, the proposal was returned to the group for modification in real-time followed by additional rounds of voting until supermajority approval was obtained.

| Statement                                                                 | Panel in Agreement |
|---------------------------------------------------------------------------|--------------------|
| 1. Skin cancer has a material impact on individual and public health.     | 7/7                |
| 2. Ultraviolet radiation is a major modifiable risk factor for skin cancer.| 7/7                |
| 3. Sun protective strategies, including the use of sunscreen, can reduce the risk of skin cancer. | 7/7                |
| 4. Adherence among the public to recommended sun protective strategies are suboptimal, especially regarding sunscreen use. | 7/7                |
| 5. To date, studies have not demonstrated that sunscreens cause harm in humans. | 7/7                |
| 6. There is insufficient evidence to show that sunscreens cause harm to marine ecosystems, including coral reefs. | 7/7                |
| 7. The proven benefits of sunscreen usage overwhelmingly outweigh the hypothetical risks. | 7/7                |

RESULTS
The expert consensus panel developed 7 statements that all received supermajority approval using a modified Delphi technique (Table 1).

1. Skin cancer has a material impact on individual and public health. 
Skin cancer (melanoma and NMSC) is the most common type of malignancy diagnosed annually, outnumbering all other cancer diagnoses ~3 to 1 with over 5.4 million new diagnoses per year and 1 in 5 Americans expected to be diagnosed with a type of skin cancer by the age of 70.1-4 The incidence of skin cancer has continued to rise in the past several decades and only recently began to plateau as public outreach on sun-safety has increased.3 However, timely diagnosis and adequate management and treatment of skin cancer still account for ~$6 billion in annual healthcare expenditures.7 Furthermore, despite improvements in care and diagnostic techniques, there are expected to be 7180 deaths in 2021 due to invasive melanoma alone.3,10

2. Ultraviolet radiation is a major modifiable risk factor for skin cancer. 
Up to 90% of melanomas can be directly attributed to ultraviolet radiation (UVR) exposure.11 Increased frequency of sunbathing has also been found to positively correlate with a greater chance of being diagnosed with NMSC.28 Artificial UVR from indoor tanning has been found to increase...
melanoma risk by as much as 20%, especially in patients under 30 years old.  

While there are multiple risk factors for skin cancer (e.g., age, gender, family history, genetics, skin phenotype), modifiable risk factors, such as degree of UVR exposure, can be mitigated during a patient’s lifetime to prevent further increase in their individual risk for skin cancer.  

UVR exposure—specifically to UVA radiation (320-400nm wavelength) and UVB (290-320 nm)—is a modifiable risk factor that has a material impact on skin cancer incidence. Studies have demonstrated chronic intermittent UVR may preferentially influence the risk of developing melanoma while chronic sustained UVR may be more related to the development of NMSC.

3. Sun protective strategies, including the use of sunscreen, can reduce the risk of skin cancer.

There are several sun protective strategies that reduce UVR exposure including wearing sunglasses, dark-colored/long-sleeved clothing, and a hat, seeking shade, wearing sunscreen with a sun protection factor of at least 30 (SPF 30+) and potentially staying indoors between 10:00 AM and 4:00 PM (depending on UVR intensity). Sunscreen remains one of the most common and effective methods of reducing UVR exposure.

Large scale, longitudinal randomized-control studies have found that daily application of SPF 15 sunscreen significantly reduced the number of clinically and histologically identified cutaneous squamous cell carcinomas (cSCC) within a 4.5 year period (Hazard ratio 0.61, 95% confidence interval 0.46-0.81) and even further specifically among histologically-confirmed cSCC (HR 0.48, 95%CI 0.35-0.64). Additional follow-up over 8 years found a consistently significant decrease in incidence of cSCC as well as a trend towards decreasing the number of basal cell carcinomas (BCC) with daily SPF 15 sunscreen. The authors noted that protection afforded by the SPF 15 sunscreen and relatively short follow-up period may have been insufficient for more thorough analysis regarding BCCs. Additional subset analysis of the original study also found a significant decrease in new primary invasive melanomas over 14.5 years (HR 0.27, 95%CI 0.08-0.97).

The sun protection factor (SPF) is a measure of a sunscreen’s “strength”, with higher SPF ratings indicating increased ability to block more UVB. The American Academy of Dermatology (AAD) recommends everyone (regardless of age, gender, or race) use broad-spectrum, water-resistant sunscreens rated SPF 30+. However data have shown higher SPF may yield additional benefits. For example, SPF 60 reduces the amount of UVR transmitted to the skin by an additional 50% compared to SPF 30, thereby reducing potential chance at mutational events, and reducing clinically significant sunburns. Split-face trials, where SPF 100 was applied to half the face and SPF 50+ applied to the other half, demonstrated significantly reduced sunburns where SPF 100 sunscreen was applied.

Of note, although concerns have also been raised that higher SPF sunscreens may provide a false sense of security and increase exposure to UVR, a randomized-controlled trial demonstrated that higher SPF sunscreens did not alter sunbathing exposure but did significantly reduce incidence of sunburn.
4. Adherence among the public to recommended sun-protective strategies are suboptimal, especially regarding sunscreen use.

Despite solar radiation being classified as a carcinogen by the World Health Organization (WHO), up to 80.6% of individuals including up to 55.3% of patients with previously diagnosed NMSC self-report poor adherence to multi-modal sun protection guidelines.49,50 Studies have found that even among patients with diagnosed melanoma, adherence to sun-protective strategies only improves transiently and then diminishes after a year, at which point it may even worsen compared to baseline.51,52

To achieve the optimal UVR protection, the US Food and Drug Administration (FDA) evaluates sunscreen applied at a density of 2 mg/cm².14 Equal protection in actual-usage settings requires approximately 1 oz of sunscreen to be applied to the entire body.13 However, under real-world conditions, patients may apply as little as 20-50% of this recommended amount.53 These figures are further diminished when considering on average not allowing enough time is given for sunscreens to settle after application (~20 minutes) prior to exposure.53 Furthermore, a majority of individuals do not re-apply sunscreen within the recommended timeframe (~2-3 hours) especially after activities that may remove sunscreen (e.g. swimming, excess friction from clothing or sand).54-56 However, some of this loss of effectiveness may be offset through the usage of higher SPF sunscreens may partially compensate for poor application technique and adherence.57,58

Underutilization is often exacerbated by additional barriers including increased application challenges, poor comprehension of the risk of extensive UVR exposure, belief that tan skin appeared healthier, belief that sunscreen was harmful to the skin, or belief that sunscreens negatively impacts systemic vitamin D levels.59

5. To date, studies have not demonstrated that sunscreens cause harm in humans.

Two small-scale randomized control trials found that, under theoretical maximal-use conditions when several organic sunscreen components were applied in excess of 2-5 times real-world amounts (2 mg/cm²) in a controlled indoor setting, serum concentrations exceeded the arbitrary “generally recognized as safe and effective” (GRASE) amount of 0.5 ng/mL proposed by the FDA.21,22 Of note, the authors of this study reported no serious treatment-emergent adverse effects and also concluded that, while further studies are suggested, their findings should not deter from the use of sunscreens.22

Inconsistent findings from animal studies, including rodent models, have raised concerns organic sunscreen agents may potential disrupt endocrine function.23 One study found pregnant rats fed oral forms of oxybenzone in excess of 1605.5-7178.5 mg/Kg had significantly reduced body weight, increased liver and kidney weight and no statistical difference in sex ratio or weights of offspring.60 A separate study found rats fed up to 1525 mg/Kg for 4 days had increased uterine weight.61 Importantly, a study determined the quantity of sunscreen required to reach equivalent body-weight standardized dose.62 At the recommended 2mg/cm² applied over the entire body surface area of an average human adult, it would take 34.6 years of daily application to reach equivalent systemic concentrations.62 However, when approximating real-world conditions in which only 50% of the
recommended amount of sunscreen (1 mg/cm²) is applied to the face, neck, hands, and arms, it would take over 277 years to achieve similar doses orally administered to rats.\textsuperscript{52}

A systematic review found only 1 randomized-control trial in humans investigating sunscreen use. This trial found no association between oxybenzone and follicle-stimulating hormone (FSH), luteinizing hormone (LH), steroid-hormone binding globulin (SHBG), testosterone, estradiol, or inhibin B after accounting for physiologic variations.\textsuperscript{63} Of the additional 10 additional human studies that were reviewed, only 2 found potential statistically—but not clinically—significant associations with oxybenzone.\textsuperscript{64,65} One study found that high maternal urine concentration of oxybenzone significantly correlated with 2.7-3.2 day decrease in gestation period during pregnancy, but did not affect birth weight nor body length.\textsuperscript{64} A prospective cohort study found maternal oxybenzone urinary concentrations were significantly associated with increased birth weight in males and decreased birth weight in females but no association with birth length.\textsuperscript{65} Importantly, neither study reported if subjects’ oxybenzone exposure was from sunscreen usage.\textsuperscript{64,65}

Studies have found that inorganic mineral agents (e.g., titanium dioxide (TiO\textsubscript{2}), zinc oxide (ZnO)) poorly penetrate the stratum corneum with less than 0.03% of ZnO nanoparticles and no TiO\textsubscript{2} able to penetrate the upper stratum corneum, thereby limiting systemic absorption.\textsuperscript{66-68} Further improvements in particle micronization have also improved cosmesis while also minimizing theoretical ability for mineral agents to induce the formation of free radicals.\textsuperscript{69-71}

Finally, randomized-controlled trials have also found no evidence that real-world sunscreen usage negatively impacted physiologic vitamin D production.\textsuperscript{73-75} For individuals who strictly adheres to ideal sun protective measures, studies have found oral vitamin D supplements provide adequate, affordable supplementation.\textsuperscript{76}

Overall, there are no studies that definitively show sunscreens including any of the 8 most common organic sunscreen agents (oxybenzone, avobenzone, octinoxate, octisalate, homosalate, octocrylene) cause systemic harms in humans.

6. There is insufficient evidence to show that sunscreens cause harm to marine ecosystems, including coral reefs.

As of January 2021, Hawaii has banned the sale of organic sunscreen agents oxybenzone and octinoxate and additional bills are being considered to ban avobenzone and octocrylene by 2023 (in the absence of a prescription).\textsuperscript{24,77} These laws follow findings suggesting organic sunscreen agents were present in seawater around Hawaii, were difficult to remove/process in wastewater, and had the potential to bleach/ossify coral reefs in vitro.\textsuperscript{78-80} Importantly, a study found that concentrations of organic sunscreen agents were materially higher in metropolitan water supplies (likely secondary to commercial/industrial run-off) than near recreational water sources.\textsuperscript{20} Furthermore, studies found that actual oxybenzone concentrations in surrounding Hawaiian seawaters to be approximately 100-1000 times less concentrated than the in vitro concentrations toxic to species of microalgae, plankton, and zebrafish.\textsuperscript{20,81-82}

Another important consideration is that potential environmental impacts of sunscreens may be confounded by other
factors, primarily climate change. Studies have demonstrated significant correlation between increasing global and ocean temperature that stress coral-algae symbiosis and stifle coral resiliency, inducing coral bleaching. Additionally, while studies have found that oxybenzone had higher concentration in fish relative to seawater, there have not been any correlation with human health. Finally, environmental-focused studies have found no evidence in real-world settings that inorganic mineral-based sunscreen agents could induce lasting damage to marine ecosystems.

Overall, there are no direct in-vivo findings suggesting that mineral-based inorganic or any of the 8 most common organic sunscreen agents (oxybenzone, avobenzone, octinoxate, octisalate, homosalate, octocrylene) cause harm to marine ecosystems.

7. The proven benefits of sunscreen usage overwhelmingly outweigh the hypothetical risks.

Studies have consistently shown that regular sunscreen usage is capable of reducing the incidence of melanoma and NMSC. Sunscreens can also prevent actinic damage and skin aging as well as ameliorate photodermatoses and photosensitive conditions. In contrast, a majority of studies proposing hypothetical risks with sunscreen usage filters in controlled settings in concentrations far beyond what is commercially available to purposefully induce pathologic responses in animal models and the environment. Under real-world conditions, these same pathologic responses have not been replicated. The panel also noted that real-world, prospective trials are simulated every weekend, on holidays, and even daily depending on local climate and season, as millions of individuals apply sunscreen without clinically appreciable adverse effects.

DISCUSSION

Sunscreens are an efficacious and integral component in the primary prevention of melanoma and NMSC. Studies have consistently shown that sunscreens are able to decrease incidence of NMSC and melanoma, with higher SPF-rated sunscreens being more capable of reducing sun burns and amount of UVR transmitted to the skin.

Unfortunately, due to a combination of inaccurate health and science literacy and misinformation campaigns, high-risk, vulnerable patients may be dissuaded from utilizing appropriate sun-protective measures, including sunscreen. Sunburns continue to be prevalent beyond the non-Hispanic White population, also affecting younger adults, patients on chronic immunosuppressive therapy and 13% of Black and 30% of Hispanic Americans. Even patients diagnosed with melanoma or NMSC have demonstrated poor long-term adherence to sun-protective measures. Frequently reported barriers to using sunscreen and sun-protective strategies include increased application challenges, cosmetic acceptability (especially with thicker products), or poor understanding of the risks of extensive UVR exposure. In the authors’ opinion, these barriers are only exacerbated by third party evaluators that potentially have a financial interest in recommending specific sunscreen products. For all of these reasons, the SCPWG believes that dermatologists are uniquely qualified to advocate for patients and educate the general public on the importance of sun-protective strategies.
The SCPWG panel also noted inconsistencies and deficiencies in some of the sunscreen literature and supports further research to cultivate evidenced-based guidelines. Future studies should evaluate the longitudinal efficacy of higher SPF sunscreens in randomized-controlled trials, especially given improvements in broad-spectrum coverage and formulations since the prior studies that demonstrated skin cancer prevention efficacy.39-41 Additionally, prospective studies in real-world settings regarding sunscreen agents and any impact they may have systemically in humans or on the environment could provide more definitive evidenced-based data to improve patient counseling.

CONCLUSION

With over 200,000 new cases melanoma and 5.4 million cases of NMSC in the US annually, accounting for over $6 billion in yearly healthcare expenditures, skin cancer poses a significant impact on both individual and public health. Primary prevention of skin cancer continues to be of utmost importance to reduce incidence, especially in melanoma prevention given over 7000 Americans continue to die annually from this cancer despite significant advancements in therapy.

As experts in the diagnosis and management of skin cancers, dermatologists are especially well-equipped to discuss with patients the risks of UVR exposure and skin cancer and benefits of multimodal sun-protective measures, including the regular and proper use of sunscreens. It is hoped that these consensus statements can serve as a basis for future health and public education initiatives. Dermatologists must continue to advocate for their patients by being involved in original investigations into the efficacy and safety of sunscreens and by educating the public on the nuances and merits of scientific findings in this space.

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Skin Cancer Prevention Working Group:
The Skin Cancer Prevention Working Group is a multi-center collaboration of experts dedicated to the prevention of skin cancer. The Working Group consists of clinical and research specialists that have spent years investigating and understanding the diagnosis and management of melanoma and non-melanoma skin cancer.

The mission of the Working Group is to cultivate and analyze evidence-based research to better understand skin cancer pathophysiology, treatment, and prevention to be leaders in skin health education.

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References:
1. Key Statistics for Basal and Squamous Cell Skin Cancer. American Cancer Society. https://www.cancer.org/cancer/basal-and-squamous-cell-skin-cancer/about/key-statistics.html. Accessed 20 April, 2021.
2. Key Statistics for Melanoma Skin Cancer. American Cancer Society. https://www.cancer.org/cancer/melanoma-skin-cancer/about/key-statistics.html. Accessed 20 April, 2021.
3. Siegel, R.L., Miller, K.D., Fuchs, H.E., Jemal, A., 2021. Cancer Statistics, 2021. CA: A Cancer Journal for Clinicians 71, 7–33.. doi:10.3322/caac.21654
4. Stern RS. Prevalence of a history of skin cancer in 2007: results of an incidence-based model. Arch Dermatol. 2010 Mar;146(3):279-82. doi: 10.1001/archdermatol.2010.4. PMID: 20231498.
5. Leiter U, Keim U, Garbe C. Epidemiology of Skin Cancer: Update 2019. Adv Exp Med Biol.
16. Wang J, Ganley CJ. Safety Threshold Considerations for Sunscreen Systemic Exposure: A Simulation Study. Clin Pharmacol Ther. 2019 Jan;105(1):161-167. doi: 10.1002/cpt.1178. Epub 2018 Aug 9. PMID: 30094825; PMCID: PMC6312469.

17. Wang, S. Q. (2011). Safety of Oxybenzone: Putting Numbers Into Perspective. Archives of Dermatology, 147(7), 865. doi:10.1001/archdermatol.2011.173

18. O'Keefe SJ, Feltis BN, Piva TJ, Turney TW, Wright PF. ZnO nanoparticles and organic chemical UV-filters are equally well tolerated by human immune cells. Nanotoxicology. 2016 Nov;10(9):1287-96. doi: 10.1080/17435390.2016.1206148. Epub 2016 Jul 19. PMID: 27345703.

19. Agin PP, Ruble K, Hermansky SJ, McCarthy TJ. Rates of allergic sensitization and irritation to oxybenzone-containing sunscreen products: a quantitative meta-analysis of 64 exaggerated use studies. Photodermatol Photoimmunol Photomed. 2008 Aug;24(4):211-7. doi: 10.1111/j.1600-0781.2008.00363.x. PMID: 1871

20. Schneider SL, Lim HW. Review of environmental effects of oxybenzone and other sunscreen active ingredients. J Am Acad Dermatol. 2019 Jan;80(1):266-271. doi: 10.1016/j.jaad.2018.06.033. Epub 2018 Nov 14. PMID: 29981751.

21. Matta MK, Zusterzeel R, Pilli NR, Patel V, Volpe DA, Florian J, Oh L, Bashaw E, Zineh I, Sanabria C, Kemp S, Godfrey A, Adah S, Coelho S, Wang J, Furlong LA, Ganley C, Michele T, Strauss DG. Effect of Sunscreen Application Under Maximal Use Conditions on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. JAMA. 2019 Jun 4;321(21):2082-2091. doi: 10.1001/jama.2019.5586. PMID: 31058986; PMCID: PMC6549296.

22. Matta MK, Florian J, Zusterzeel R, Pilli NR, Patel V, Volpe DA, Yang Y, Oh L, Bashaw E, Zineh I, Sanabria C, Kemp S, Godfrey A, Adah S, Coelho S, Wang J, Furlong LA, Ganley C, Michele T, Strauss DG. Effect of Sunscreen Application on Plasma Concentration of Sunscreen Active Ingredients: A Randomized Clinical Trial. JAMA. 2020 Jan 21;323(3):256-267. doi: 10.1001/jama.2019.20747. Erratum in: JAMA. 2020 Mar 17;323(11):1098. PMID: 31961417; PMCID: PMC6990686.

23. Ghazipura M, McGowan R, Arslan A, Hossain T. Exposure to benzophenone-3 and reproductive toxicity: A systematic review of human and animal studies. Reprod Toxicol. 2017 Oct;73:175-183. doi: 10.1016/j.reprotox.2017.08.015. Epub 2017 Aug 24. PMID: 28844799.

24. Ouchene L, Litvinov IV, Netchiporouk E. Hawaii and Other Jurisdictions Ban Oxybenzone or Octinoxate Sunscreens Based on the Confirmed Adverse Environmental Effects of Sunscreen Ingredients on Aquatic Environments. J Cutan Med Surg. 2019 Nov/Dec;23(6):648-649. doi: 10.1177/1203475419871592. PMID: 31729915

25. Hsu C-C, Sandford BA. The Delphi technique: making sense of consensus. Practical assessment, research & evaluation 2007;12:1-8

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26. Richard MA, Barnetche T, Rouzaud M, et al. Evidence-based recommendations on the role of dermatologists in the diagnosis and management of psoriatic arthritis: systematic review and expert opinion. J Eur Acad Dermatol Venereol 2014;28(s5):3-12.

27. Gottlieb AB, Levin AA, Armstrong AW, et al. The International Dermatology Outcome Measures Group: formation of patient-centered outcome measures in dermatology. J Am Acad Dermatol 2015;72(2):345-8.

28. Larese Filon, F., Buric, M., & Fluehler, C. (2018). Photodermatology, Photoimmunology & Photomedicine. doi:10.1111/phpp.12417

29. Ghiasvand R, Rueegg CS, Weiderpass E, et al. Indoor tanning and melanoma risk: long-term evidence from a prospective population-based cohort study. Am J Epidemiol 2017;185(3):147-56.a

30. Carr S, Smith C, Wernberg J. Epidemiology and Risk Factors of Melanoma. Surg Clin North Am. 2020 Feb;100(1):1-12. doi: 10.1016/j.suc.2019.09.005. Epub 2019 Nov 4. PMID: 31753105.

31. Kim DP, Kus KJB, Ruiz E. Basal Cell Carcinoma Review. Hematol Oncol Clin North Am. 2020 Jan 28;34(2):373-87. doi:10.1016/j.honc.2018.09.004. PMID: 30497670.

32. Gilaberte Y, Casanova JM, Garcia-Malinis AJ, Arias-Santiago S, Garcia de la Fuente MR, Pamiés-Gracia M, Ramirez-Palomino J, Ruiz-Campos I, Gracia-Cazaña T, Buendia-Eisman A. Skin Cancer Prevalence in Outdoor Workers of Ski Resorts. J Skin Cancer. 2020 Jan 28;2020:8128717. doi: 10.1155/2020/8128717. PMID: 30497670.

33. Heltloft KN, Slagor RM, Agner T, Bonde JP. Metal arc welding and the risk of skin cancer. Int Arch Occup Environ Health. 2017 Nov;90(8):873-881. doi: 10.1007/s00420-017-1248-5. Epub 2017 Aug 1. PMID: 28766013; PMCID: PMC5640727.

34. Nadhan KS, Chung CL, Buchanan EM, Shaver C, Shipman S, Allawh RM, Hoffman ML, Lim G, Abdelmalek M, Cusack CA. Risk factors for keratinocyte carcinoma skin cancer in nonwhite individuals: A retrospective analysis. J Am Acad Dermatol. 2019 Aug;81(2):373-378. doi: 10.1016/j.jaad.2019.01.038. Epub 2019 Jan 2

35. Suppa M, Gandini S, Njimi H, Bulliard JL, Correia O, Duarte AF, Peris K, Stratigos AJ, Nagore E, Longo M, Bylaiie-Bucinskiene M, Karls R, Helppikangas H; Euromelanoma Working Group,, Del Marmol V. Association of sunbed use with skin cancer risk factors in Europe: an investigation within the Euromelanoma

36. Nagore E, Hueso L, Botella-Estrada R, et al. Smoking, sun exposure, number of nevi and previous neoplasias are risk factors for melanoma in older patients (60 years and over). J Eur Acad Dermatol Venereol 2010;24(1):50-7.

37. Schmitt J, Seidler A, Diepger TL, et al. Occupational ultraviolet light exposure increases the risk for the development of cutaneous squamous cell carcinoma: a systematic review and meta-analysis. Br J Dermatol 2011;164(2):291-307.

38. Li H, Colantonio S, Dawson A, Lin X, Beecker J. Sunscreen Application, Safety, and Sun Protection: The Evidence. J Cutan Med Surg. 2019 Jul/Aug;23(4):357-369. doi: 10.1177/1203475419856611. Epub 2019 Jun 20. PMID: 31219707.

39. Green A, Williams G, Neale R, Hart V, Leslie D, Parsons P, Marks GC, Gaffney P, Battistutta D, Frost C, Lang C, Russell A. Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. Lancet. 1999 Aug 28;

40. van der Pols JC, Williams GM, Pandeya N, Logan V, Green AC. Prolonged prevention of squamous cell carcinoma of the skin by regular sunscreen use. Cancer Epidemiol Biomarkers Prev. 2006 Dec;15(12):2546-8. doi: 10.1158/1055-9965.EPI-06-0352. Epub 2006 Nov 28. PMID: 17132769.

41. Green AC, Williams GM, Logan V, Strutton GM. Reduced melanoma after regular sunscreen use: randomized trial follow-up. J Clin Oncol. 2011 Jan 20;29(3):257-63. doi: 10.1200/JCO.2010.28.7078. Epub 2010 Dec 6. PMID: 2135266.

42. Sun Protection Factor (SPF). FDA Center for Drug Evaluation and Research. https://www.fda.gov/about-fda/center-drug-evaluation-and-research-cder/sun-protection-factor-spf. Accessed 23 April 2021.

43. Mancuso, J.B., Maruthi, R., Wang, S.Q. et al. Sunscreens: An Update. Am J Clin Dermatol 18, 643–650 (2017). https://doi.org/10.1007/s40257-017-0290-0

44. Kohli I, Nicholson CL, Williams JD, Lyons AB, Seo I, Maitra P, Tian X, Atillasoy E, Lim HW, Hamzavi IH, Greater efficacy of SPF 100+ sunscreen compared to SPF 50+ in sunburn prevention during five consecutive days of sunlight exposure: A Randomized, Double-Blind Clinical Trial, Journal of the American Ac

45. Williams JD, Maitra P, Atillasoy E, Wu MM, Farberg AS, Rigel DS. SPF 100+ sunscreen is more protective against sunburn than SPF 50+ in actual use: Results of a randomized, double-blind, split-face, natural sunlight exposure clinical trial. J Am Acad Dermatol. 2018 May;78(5):902-910.e2. doi: 10.1016/j.jaad.2018.04.029

46. Autier P, Doré JF, Négrier S, Liénard D, Panizzon R, Lejeune FJ, Guggisberg D, Eggermont AM. Sunscreen use and duration of sun exposure: a double-blind, randomized trial. J Natl Cancer Inst. 1999 Aug 4;91(15):1304-9. doi: 10.1093/jnci/91.15.1304. PMID: 10433619.
47. Autier P, Doré JF, Reis AC, et al. Sunscreen use and intentional exposure to ultraviolet A and B radiation: a double blind randomized trial using personal dosimeters. Br J Cancer. 2000;83(9):1243-1248. doi: 10.1054/bjoc.2000.1429

48. Dupuy A, Dunant A, Grob JJ; Réseau d’Épidémiologie et Dermatologie. Randomized controlled trial testing the impact of high-protection sunscreens on sun-exposure behavior. Arch Dermatol. 2005 Aug;141(8):950-6. doi: 10.1001/archderm.141.8.950. PMID: 16103322.

49. Ultraviolet radiation. Global Health Observatory (GHO) data. https://www.who.int/gho/phe/ultraviolet_radiation/en/##-text=One%20in%20every%20three%20cancers recently%20from%20artificial%20tanning%20sunb eds. Accessed 26 April 2021.

50. Fischer AH, Wang TS, Yenokyan G, Kang S, Chien AL. Sunburn and sun-protective behaviors among adults with and without previous nonmelanoma skin cancer (NMSC): A population-based study. J Am Acad Dermatol. 2016 Aug;75(2):371-379.e5. doi: 10.1016/j.jaad.2016.02.1236. Epub 2016 May 16. PMID: 27198078; PMCID: PMC5187208.

51. Novak CB, Young DS, Lipa J, Cole C, Appa Y, Rigel DS. A comparison of sunscreen user protection factors (SPF) to ultraviolet protection factor sunscreens (>=70) may provide ultraviolet protection above minimal recommended levels by adequately compensating for lower sunscreen user application amounts. J Am Acad Dermatol 2013; 69: 481–483.

52. Russak J, Chen T, Appa Y, Rigel DS. A comparison of sunburn protection of high-sun protection (SPF) sunscreen: SPF85 sunscreen is significantly more protective than SPF50. J Am Acad Dermatol 2010; 62: 348–349

53. Nahar VK, Wilkerson AH, Pearlman RL, Ferris TS, Zardoost P, Payson SN, Aman I, Quadri SSA, Brodell RT. Skin cancer-related knowledge, attitudes, beliefs, and practices among the population in Gulf Cooperation Council countries: a systematic search and literature review. Arch Dermatol Res. 2020 Oct;312(8)

54. Nakamura N, Inselman AL, White GA, Chang CW, Trbojevich RA, Sepher E, Voris KL, Patton RE, Bryant MS, Harrouk W, McIntyre BS, Foster PM, Hansen DK. Effects of maternal and lactational exposure to 2-hydroxy-4-methoxybenzophenone on development and reproductive organs in male and female rat offspring. Birth Defects Reprod Toxicol. 2015 Feb;104(1):35-51. doi: 10.1002/bdrb.21137. Epub. Birth Defects Res B Dev Reprod Toxicol. 2015 Jun;104(3):140. PMID: 25707689; PMCID: PMC4353586.

55. Schlumpf M, Cotton B, Conscience M, Haller V, Steinmann B, Lichtensteiger W. In vitro and in vivo estrogenicity of UV screens [published correction appears in Environ Health Perspect. 2001 Nov;109(11):A517]. Environ Health Perspect. 2001;109(3):239-244. doi:10.1289/ehp.01109239.

56. Wang SQ, Burnett ME, Lim HW. Safety of oxybenzone: putting numbers into perspective. Arch Dermatol. 2011 Jul;147(7):865-6. doi: 10.1001/archdermatol.2011.173. PMID: 21768493.

57. Janjua NR, Mogensen B, Andersson AM, Petersen JH, Henriksen M, Skakkebaek NE, Wulf HC. Systemic absorption of the sunscreens benzophenone-3, octyl-methoxycinnamate, and 3-(4-methyl-benzylidene) camphor after whole-body topical application and reproductive hormone levels in humans. J Invest Dermatol. 2004

58. Tang R, Chen MJ, Ding GD, Chen XJ, Han XM, Zhou K, Chen LM, Xia YK, Tian Y, Wang XR. Associations of prenatal exposure to phthalates and birth outcomes. Environ Pollut. 2013 Jul;178:115-20. doi: 10.1016/j.envpol.2013.03.023. Epub 2013 Apr 3. PMID: 23562958.

59. Wolff MS, Engel SM, Berkowitz GS, Ye X, Silva MJ, Zhu C, Wemmur J, Calafat AM. Prenatal phenol and phthalate exposures and birth outcomes. Environ Health Perspect. 2008 Aug;116(8):1092-7. doi: 10.1289/ehp.11007. PMID: 18709157; PMCID: PMC2516577.

60. Schneider SL, Lim HW. A review of inorganic UV filters: zinc oxide and titanium dioxide. Photomed. 2014 Apr;3:101. doi:10.1289/ehp.01109239.

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67. Nash JF. Human safety and efficacy of ultraviolet filters and sunscreen products. Dermatol Clin 2006; 24: 35–51.
68. Filipe P, Silva JN, Silva R, et al. Stratum corneum is an effective barrier to TiO2 and ZnO nanoparticle percutaneous absorption. Skin Pharmacol Physiol 2009;22:266-75
69. Rai R, Shanmuga SC, Srinivas C. Update on photoprotection. Indian J Dermatol 2012;57:335-42.
70. G. J. Nohynek and E. K. Dufour. Nano-sized cosmetic formulations or solid nanoparticles in sunscreens: a risk to human health?, Arch. Toxicol., 2012, 86, 1063–1075.
71. K. Schilling, B. Bradford, D. Castelli, E. Dufour, J. F. Nash, W. Pape, et al., Human safety review of “nano” titanium dioxide and zinc oxide, Photochem. Photobiol. Sci., 2010, 9, 495–509.
72. S. L. Schneider and H. W. Lim. A review of inorganic UV filters zinc oxide and titanium dioxide, Photodermatol., Photoinmunol. Photomed., 2018, 442–446
73. Neale RE, Khan SR, Lucas RM, Waterhouse M, Whiteman DC, Olsen CM. The effect of sunscreen on vitamin D: a review. Br J Dermatol. 2019 Nov;181(5):907-915. doi: 10.1111/bjd.17980. Epub 2019 Jul 9. PMID: 30945275.
74. Jayaratne N, Russell A, van der Pols JC. Sun protection and vitamin D status in an Australian subtropical community. Prev Med. 2012 Aug;55(2):146-50. doi: 10.1016/j.ypmed.2012.05.011. Epub 2012 May 23. PMID: 22634425.
75. Marks R, Foley PA, Jolley D, Knight KR, Harrison J, Thompson SC. The effect of regular sunscreen use on vitamin D levels in an Australian population. Results of a randomized controlled trial. Arch Dermatol. 1995 Apr;131(4):415-21. PMID: 7726582.
76. Lim HW, Gilchrest BA, Cooper KD, Bischoff-Ferrari HA, Rigel DS, Cyr WH, Miller S, DeLeo VA, Lee TK, Demko CA, Weinstock MA, Young A, Edwards LS, Johnson TM, Stone SP. Sunlight, tanning booths, and vitamin D. J Am Acad Dermatol. 2005 May;52(5):686-76. doi: 10.1016/j.jaad.2005.03.015. Erratum in: J Am Acad Dermatol.
77. Relating To Sunscreens, HB102 HD1, 31st Legislature. (2021). https://www.capitol.hawaii.gov/measure_indiv.aspx?billtype=HB&billnumber=102&year=2021
78. Balmer ME, Buser HR, Müller MD, Poiger T. Occurrence of some organic UV filters in wastewater, in surface waters, and in fish from Swiss Lakes. Environ Sci Technol. 2005 Feb 15;39(4):953-62. doi: 10.1021/es040055r. PMID: 15773466.
79. Brausch JM, Rand GM. A review of personal care products in the aquatic environment: environmental concentrations and toxicity. Chemosphere. 2011 Mar;82(11):1518-32. doi:
10.1016/j.chemosphere.2010.11.018. Epub 2010 Dec 23. PMID: 21185057.
80. Downs CA, Kramarsky-Winter E, Segal R, Fauth J, Knutson S, Bronstein O, Ciner FR, Jeger R, Lichtenfeld Y, Woodley CM, Pennington P, Cadenas K, Kushmaro A, Loya Y. Toxicopathological Effects of the Sunscreen UV Filter, Oxybenzone (Benzophenone-3), on Coral Planulae and Cultured Primary Cells and Its Environmental Contamination in Hawaii and the U.S. Virgin Islands. Arch Environ Contam Toxicol. 2016 Feb;70(2):265-88. doi: 10.1007/s00244-015-0227-7. PMID: 26487337.
81. Du Y, Wang WQ, Pei ZT, Ahmad F, Xu RR, Zhang YM, Sun LW. Acute Toxicity and Ecological Risk Assessment of Benzophenone-3 (BP-3) and Benzophenone-4 (BP-4) in Ultraviolet (UV)-Filters. Int J Environ Res Public Health. 2017 Nov 19;14(11):1414. doi: 10.3390/ijerph14111414. PMID: 29156601; PMCID: PMC5708053.
82. Mitchelmore CL, He K, Gonsior M, Hain E, Heyes A, Clark C, Younger R, Schmitt-Kopplin P, Feerick A, Conway A, Blaney L. Occurrence and distribution of UV-filters and other anthropogenic contaminants in coastal surface water, sediment, and coral tissue from Hawaii. Sci Total Environ. 2019 Jun 20;670:398-4.
83. Cheng L, Abraham J, Hausfather Z, Trenberth KE. How fast are the oceans warming? Science. 2019 Jan 11;363(6423):128-129. doi: 10.1126/science.aav7619. Erratum in: Science. 2019 Mar 8;363(6431): PMID: 30630919.
84. Stattery M, Pankey MS, Lesser MP. Annual Thermal Stress Increases a Soft Coral’s Susceptibility to Bleaching. Sci Rep. 2019 May 30;9(1):8064. doi: 10.1038/s41598-019-44566-9. PMID: 31147567; PMCID: PMC6542812.
85. Authority GBRMP, Final report: 2016 coral bleaching event on the Great Barrier Reef, GBRMPA, Townsville, 2017.
86. Gago-Ferrero P, Díaz-Cruz MS, Barceló D. An overview of UV-absorbing compounds (organic UV filters) in aquatic biota. Anal Bioanal Chem. 2012 Nov;404(9):2597-610. doi: 10.1007/s00216-012-6067-7. Epub 2012 Jun 6. PMID: 22669305.
87. Hughes MC, Williams GM, Baker P, Green AC. Sunscreen and prevention of skin aging: a randomized trial. Ann Intern Med. 2013 Jun 4;158(11):781-90. doi: 10.7326/0003-4819-158-11-201306040-00002. PMID: 23732711.
88. Schleyer V, Weber O, Yazdi A, Benedix F, Dietz K, Röcken M, Berneburg M. Prevention of polymorphic light eruption with a sunscreen of very high protection level against UVB and UVA radiation under standardized photodiagnostic conditions. Acta Derm Venereol. 2008;88(6):555-60. doi: 10.2340/00015555-0509.
89. Oakley AM, Badri T, Harris BW. Photosensitivity. 2020 Aug 10. In: StatPearls [Internet]. Treasure
90. Glazer, A. M., Svoboda, R. M., Teplitz, R. W., & Rigel, D. S. (2018). Editorial: Overcoming Consumer Challenges in Sunscreen Selection. SKIN The Journal of Cutaneous Medicine, 2(3), 168–171. https://doi.org/10.25251/skin.2.3.3

91. Prado G, Svoboda RM, Teplitz RW, Farberg AS, Rigel DS. Patient knowledge of FDA-mandated sunscreen labeling terminology: A cross-sectional survey. Photodermatol Photoimmunol Photomed. 2019 May;35(3):141-147. doi: 10.1111/phpp.12437. Epub 2018 Nov 22. PMID: 30383894.

92. Holman DM, Ding H, Guy GP Jr, Watson M, Hartman AM, Perna FM. Prevalence of Sun Protection Use and Sunburn and Association of Demographic and Behavioral Characteristics With Sunburn Among US Adults. JAMA Dermatol. 2018 May 1;154(5):561-568. doi: 10.1001/jamadermatol.2018.0028. PMID: 29541756; PMCID: PMC

93. Tabatabaie S, Litt JS, Crane LA. The experience of outdoor physical activity for skin cancer survivors: understanding the importance of the built and natural environments. J Cancer Surviv. 2020 Oct;14(5):739-756. doi: 10.1007/s11764-020-00889-5. Epub 2020 Jun 6. PMID: 32506221.

94. Varedi, A., Wu, Y. P., Klein, S. Z., Leachman, S. A., & Grossman, D. (2018). Mineral sunscreens not recommended by Consumer Reports: What lies beneath the surface? Journal of the American Academy of Dermatology. doi:10.1016/j.jaad.2018.09.009

95. Cartee TV, Alam M, Armbrrecht ES, Behera A, Lawrence N, Bordeaux JS, Baum CL, Rossi A, Maher IA. Patient-Centered Outcomes for Skin Cancer Management: Utilization of a Patient Delphi Process to Identify Important Treatment Themes. Dermatol Surg. 2019 Feb;45(2):246-253. doi: 10.1097/DSS.0000000000001756. P

96. Jin J. Behavioral Counseling for Skin Cancer Prevention. JAMA. 2018 Mar 20;319(11):1176. doi: 10.1001/jama.2018.1624. PMID: 29558553.