Feature Article

Journal of Cutaneous Medicine and Surgery
1–13

DOI: 10.1177/1203475419856611
jcms.sagepub.com

Canadian Dermatology Association · Association canadienne de dermatologie

Sunscreen Application, Safety, and Sun Protection: The Evidence

Heidi Li[1], Sophia Colantonio[1,2], Andrea Dawson[1,2], Xing Lin[1,2], and Jennifer Beecker[1,2]

Abstract

Recently in Canada, there has been an effort to create consistent messaging about sun safety as there is a lack of up-to-date evidence-based guidelines regarding sun-protection measures. This review aimed to provide updated, evidence-based recommendations on sunscreen application, safety, and sun protection regarding the following topics for which there is clinical uncertainty: physical barriers, sunscreen properties, sunscreen application, and risk-benefit analysis.

Keywords

application, guidelines, photodamage, photoprotection, review, skin cancer, SPF, sun protection, sun protection factor, sunscreen

Introduction

Skin cancer is the most common form of cancer in Canada, with non–melanoma skin cancer (NMSC) alone accounting for at least 40% of new cancer cases.[1] In 2014, an estimated 6500 new cases of melanoma and 76 100 cases of NMSC occurred in Canada. The incidence of skin cancer is projected to rise in the coming decades because of the aging population.[2] Since most skin cancers are preventable by reducing natural and artificial ultraviolet (UV) radiation exposure,[3] public education on and advocacy for sun protection are essential. Two key messages regarding sun-safety education are the regular use of sunscreen and physical protective agents, such as clothing, hats, sunglasses, and shade.[4]

Sunscreens have gained tremendous commercial success since their introduction in the United States in 1928 and have been incorporated into various moisturizers, makeup, and lip products. Worldwide, sun-care product sales have increased 7% on average per year over the last 5 years.[4]

The efficacy of protection by sunscreens has been widely accepted as indicated by the sun protection factor (SPF), first adopted in 1978 by the US FDA. In Canada, sunscreens are approved and regulated by Health Canada. To promote uniformity of public health messages in Canada, a National Consensus on Sun Safety Messages was developed in 2016.[5] In addition, the FDA and Health Canada alike have modified their sunscreen monographs in the past 5 years.

The purpose of this study was to assess the current literature on sun-protection measures and methods to derive a set of best-practice recommendations.

Methods

Literature Search

A list of broad topics on sunscreen use and sun-protection methods was formulated after a preliminary survey between the authors and members of the Dermatology Division at The Ottawa Hospital, a Canadian tertiary care hospital. The proposed topics included “sunscreen application amount,” “application frequency,” “application timing,” “SPF recommendation,” “formulation of sunscreens,” “organic vs inorganic sunscreens,” “water-resistance of sunscreens,” “lip protection,” “physical barriers,” “population factors for sunscreen use,” and “harms and benefits of sunscreens.”

A search for relevant studies in MEDLINE (1946 to December 2018) was performed. Our search strategy used all combinations of the following key terms: “sunscreening agents,” “application,” “skin pigmentation,” “administration,” “protective clothing,” “sunburn,” “water resist,” “sunburn,” “sun protection factor,” “skin neoplasms,” “skin aging,” “photoaging,” and “lip.” Publications were limited to meta-analyses, systematic reviews, randomized controlled trials, guidelines, comparative studies, evaluation studies, or

[1]University of Ottawa, ON, Canada
[2]Division of Dermatology, The Ottawa Hospital, ON, Canada

Corresponding Author:
Jennifer Beecker, The Ottawa Hospital, The Division of Dermatology, 737 Parkdale Ave, 4th Floor, Parkdale Clinic, Ottawa, ON K1Y 4E9, Canada.
Email: jbeecker@toh.ca

multicentre studies in the English language after 1946. A manual search was also conducted based on references cited in selected articles generated by the literature search.

Research Questions

The abstracts and titles of articles yielded from the search were screened to select relevant articles that addressed the following research questions for subsequent full-text review:

1. **Physical barriers**
   a. Is UV protective clothing superior to regular clothing?
   b. What minimum level of UV protection is needed in sunglasses?
2. **Sunscreen properties**
   a. What is the recommended SPF of sunscreens?
   b. What is the preferred vehicle of sunscreens?
   c. Should inorganic or organic sunscreens be used?
   d. When should water-resistant sunscreens be used?
   e. Lip protection
   f. Expiry date
3. **Sunscreen application**
   a. What amount of sunscreen is appropriate to apply?
   b. How frequently should sunscreen be reapplied? Does physical activity affect the frequency of application?
   c. How long before sun exposure should sunscreen be applied?
   d. Does application of sunscreen vary for different skin types?
4. **Risk-benefit analysis**
   a. Is sunscreen harmful (ie, risks of compounds/ingredients)?
   b. Are sunscreens safe for infants?
   c. Does sunscreen prevent skin damage/aging/wrinkles?
   d. Does sunscreen prevent skin cancer?

Critical Appraisal and Recommendation

The research design and quality of all relevant publications were assessed using the Canadian Task Force on Preventive Health Care (CTFPHC) grading of recommendations, assessment, development, and evaluation (GRADE) definitions (see Supplementary Tables 1 and 2).[6] The levels of evidence for all articles included in the systemic review are presented in Supplementary Table 3. Studies relevant to the same topic were evaluated together to derive an overall recommendation. The level of evidence for each recommendation was ranked based on the CTFPHC GRADES of Recommendation as "strong" or "weak" (see Table 1).[6]

Results

The initial search yielded 424 studies. After screening the titles and abstracts for relevance, 84 articles were selected for full-text review, as summarized in Supplementary Table 4. Here, we review the evidence for each research question to support the recommendations summarized in Table 1.

Physical Barriers

Is Ultraviolet Protective Clothing Superior to Regular Clothing?

Protective clothing is a simple method of photoprotection.[7] Canadian consumer guidelines for UV protection clothing refer to the ultraviolet protection factor (UPF), a standardized in vitro measurement of the ultraviolet A (UVA) and ultraviolet B (UVB) protection of clothing.[8] Currently, UPFs 15 and 20 are rated as good photoprotection; UPF 25, 30, and 35 as very good; and UPF 40, 45, 50, and 50+ as excellent. There are no Canadian guidelines as to the ideal minimum UPF factor, whereas European standards recommend UPF 40+.

UPF ratings are affected by multiple heterogeneous factors, including weave density, composition, colour, fabric thickness, stretch, moisture, and fabric condition.[9] Two studies[10,11] have demonstrated that thicker and heavier-weight clothing with dark colourants provided more protection. Similarly, an in vitro study[12] found that UPF of a replica England football shirt with white vertical bands of varying thickness had a UPF of 5 for the thinner bands and 11 for the thicker bands, highlighting the importance of clothing thickness. For fabric composition, numerous studies demonstrated that Lycra/elastane fabrics were the most likely to have UPFs of 50 or higher, followed by plastic, nylon, and polyester.[9] Thus, it is important for consumers to check the UPF tag when selecting garments for UV-protection purposes. If UPF tags are not available, generally consumers should choose garments with greater fabric weight, thickness, tighter weave, darker colours, and those of made of Lycra/polyester, as these characteristics typically result in greater photoprotection.[7] Additionally, consumers should be aware that garments that are worn thin, wet, or stretched may offer reduced UV protection as UPF values decreases with stretch, wetness, and numerous washes.[7]

Although all types of clothing provide some degree of UV-light protection, recent studies have demonstrated that some regular clothing garments do not provide sufficient UV protection.[13] UV-protective clothing is specifically designed to block out UV light and may provide more effective broad-spectrum photoprotection. Numerous studies, including two in vitro studies[14,15] found that athletic clothing (yellow soccer jersey, blue shorts, sweatshirt, baseball cap, cycling jerseys) all offered excellent protection. There are only a few studies comparing the photoprotection of regular clothing with that of photoprotective clothing. A small study[16] demonstrated that regular clothing provided similar UVA/UVB protection as photoprotective clothing, although their study

Table 1. Summary of Recommendations for Each Research Question and Strength of Recommendations as Evaluated Using the CTFPHC GRADE System.

Research Question	Recommendation	Strength
Physical Barriers	UV protective clothing is superior to regular clothing as it provides excellent consistent light-weight photoprotection with clear UPF ratings.	Weak
	When choosing regular clothing items with no UPF tags, choose garments with tighter weaves, increased fabric weight, thickness, darker colours, and Lycra/polyester composition and that cover more skin. Moisture, fabric stretching, and fabric degradation could also decrease the UPF factor.	Strong
	Sunglasses that provides UV absorption up to 400 nm should be worn during daily activities (eg, driving) in conjunction with hats. In particular, this message should be reinforced with men and minorities, the most at-risk groups.	Weak
SPF	A broad-spectrum sunscreen with UVA and UVB filters and SPF of at least 30 should be applied, and even higher SPF sunscreens may be used to compensate for common underapplication of sunscreen.	Strong
	Patient education is needed on the meaning of SPF and other factors affecting effectiveness of sunscreen apart from the SPF value alone.	Strong
Vehicle of Sunscreen	Water-in-oil emulsion is the recommended formulation of sunscreens to achieve highest SPF and water resistance.	Weak
Organic vs Inorganic Sunscreens	A broad-spectrum sunscreen containing a balance of UVA and UVB filters is recommended, regardless of whether the components are organic or inorganic.	Strong
	When using sunscreens with primarily nonmicronized inorganic filters, education to avoid underapplication is especially important.	Strong
Water Resistance	Water-resistant sunscreen (for 40 or 80 minutes) should be worn in conditions in which there is significant sweating, water immersion, increased skin friction via physical contact, or contact with sand.	Strong
Lip Protection	Lip sunscreen should be applied generously to cover the whole lip.	Strong
	High-SPF products (≥ 30) and reapplication should be used to compensate for underapplication.	Strong
Expiry Date	Do not use sunscreens that are past the manufacturer-specified expiry date or recommended period after opening. Sunscreens should be stored at room temperature to ensure stability.	Weak
Sunscreen Application	Apply liberally (approximately 45 ml) to all exposure areas.	Strong
	Reapplication within an 8-hour period is necessary only after activities that may remove the sunscreen layer (swimming, sweating, friction).	Strong
	Apply prior to sun exposure and at least 20 minutes prior to water activities.	Weak
	Individuals of colour should use photoprotection, including sunscreen.	Weak
Sunscreen Safety	Safe overall with a favourable risk-benefit profile.	Strong
	Stratum corneum is an effective barrier, thus systemic absorption should not be a concern.	Strong
	Risks: photoallergy (most common, but rare), reproductive toxicity, decreased fertility (lack of evidence), hazardous to coral (more research needed; direct association with sunscreen not established).	Strong
	Limit the use of sunscreen in children younger than age 6 months.	Weak
Benefits	Sunscreen prevents photoaging.	Strong
	Sunscreen prevents melanoma and non–melanoma skin cancer.	Strong

Abbreviations: CTFPHC, Canadian Task Force on Preventive Health Care; GRADE, grading of recommendations, assessment, development, and evaluation; SPF, sun protection factor; UPF, ultraviolet protection factor; UV, ultraviolet; UVA, ultraviolet A; UVB, ultraviolet B

was very limited in terms of the number and type of garments tested. Furthermore, UV-protective clothing is also designed to be more lightweight and breathable compared with normal clothing, making it the ideal consumer choice for hot summer weather and outdoor physical activities. Although certain items of normal clothing such as denim jeans provide a high UPF (1700), they are not practical for athletic activities.[9] Although the evidence is limited, UPF clothing provides excellent photoprotection with few disadvantages other than cost, whereas typical normal clothing may provide inadequate to excellent protection.

Recommendation: There is fair evidence to support the use of photoprotective clothing as it provides excellent consistent photoprotection with clear UPF ratings, allowing the consumer to know the exact amount of photoprotection offered. Although certain regular clothing items may provide comparable photoprotection, regular clothing is more variable with a broader spectrum of photoprotection ranging from inadequate to excellent, making it potentially difficult for the consumer to definitively evaluate the photoprotection offered. In addition, as it may be difficult to make regular clothing lightweight, photoprotective clothing is an ideal choice for consumers in hot summer weather, if affordable. When choosing regular clothing items with no UPF tags, consumers should choose garments with tighter weaves, increased fabric weight, thickness, darker colours, and of Lycra/polyester composition and that cover more skin. A practical tip to assess regular clothing is to hold the garment up to a light source to see whether the light shines through. Consumers should also be aware that moisture, fabric stretching, and fabric degradation decrease the UPF factor. Further studies that compare a variety of UPF clothing and normal clothing under different conditions are needed.

Grade of Recommendation: STRONG

Minimum Protection in Sunglasses. Chronic UV radiation (UVR) is a known risk factor for cataracts, age-related macular degeneration, and pterygium.[2] There is also the risk of skin cancer involving the delicate skin adjacent to the eye that is typically not protected by sunscreen. The Canadian sunglass industry is self-regulated, and manufacturers comply with voluntary standards when classifying their sunglasses as cosmetic (block 0%-60% visible light and UVA and 87.5%-95% of UVB), general purpose for daily activities (block 60%-92% visible and UVA and 95%-99% of UVB), or special purpose, ie, for skiing (block up to 97% of visible light, up to 98.5% of UVA, and at least 99% of UVB rays), as outlined in Health Canada 2010 guidelines. However, Dain et al.[17] demonstrated that 17% of the 646 pairs of sunglasses tested failed to meet voluntary standards, despite being labelled as such.

Health Canada 2010 guidelines recommend only general-purpose sunglasses for driving and special-purpose glasses for prolonged sun exposure. General-purpose sunglasses are often marketed as "UV absorption up to 400 nm," the equivalent of 100% UV absorption.

Ophthalmologists and optometrists also recommend the combination of a hat with sunglasses to minimize light from entering from the side or top of sunglass frames and then reflecting off the inner surface of the lens and into the eye.[18] A study by Sliney et al[19], using simulated ocular geometry, demonstrated that the human eye receives at least 5% of the UVR dose when wearing clear lenses opaque to the UVR because of the lack of protection above and to the sides of sunglasses. This is also why the "wrap-around" style of sunglasses is often recommended.

Patients should be aware that darker sunglasses do not necessarily provide superior ocular UV protection, as darker glasses could result in greater pupil dilation and increased UV exposure to the lens.[2]

Culture may influence sunglasses usage; this may be a consideration for targeted sun-awareness campaigns. A cross-sectional study of US postal workers[20] found that visible minorities and men were significantly less likely to wear sunglasses than Caucasians and women, respectively. 63% of Caucasians vs 44% of visible minorities reported always wearing sunglasses, and women were 78% more likely to wear sunglasses than men.[21] A systematic review[22] found that sunglasses were the most commonly reported sun-protective behaviour of outdoor workers; however, this varied widely between groups of workers as 80% of lifeguards wore sunglasses compared with British or Japanese construction workers, who rarely wore sunglasses.

Recommendation: For daily activities, patients should wear general-purpose sunglasses in conjunction with a broad-brimmed hat to reduce the amount of UVR reaching the eyes. Better-quality studies are needed to further quantify the absolute risk reduction of wearing sunglasses and in combination with broad-brimmed hats. Physicians should specifically emphasize the importance of sunglasses to groups who are most at risk, namely individuals who experience high-UV occupational exposure as well as men and minorities. Greater efforts should be made to simplify labelling so patients can easily identify the purpose of sunglasses (cosmetic, general purpose, or special activity).

Grade of Recommendation: STRONG

Sunscreen Properties

What is the Recommended Sun-Protection Factor of Sunscreens?

History of Sun-Protection Factor and Increasing Sun-Protection Factor. The ideal SPF to recommend to the public has been difficult to define. The Canadian Dermatology Association (CDA) currently recommends using broad-spectrum sunscreens with SPF values of 30 or higher. This message is now echoed throughout Canada based on the National Consensus Process on Recommended Core Content for Sun Safety Messages in Canada.

Although there is a common misconception that SPF values are multiplicative (SPF 30 sunscreen is in fact not twice as effective compared with SPF 15), there is abundant evidence suggesting that higher SPF is indeed more effective at sun protection. A randomized, double-blind, split-face, natural sunlight exposure clinical trial[23] demonstrated that SPF 100+ sunscreen was significantly more effective in protecting against sunburn than SPF 50+ sunscreen, with 55.3% of their participants more sunburned on the SPF 50+ protected side compared with 5% on the SPF 100+ protected side. In addition, 40.7% exhibited increased erythema scores on the SPF 50+ -protected side as compared with 13.6% on the SPF 100+-protected side. Similarly, Russak and colleagues demonstrated statistically significantly lower cases of sunburn with application of SPF 85 sunscreen compared with SPF 50[24] and Pissavini and Diffey showed that SPF 30 application had only 11% of skin exhibiting erythema as compared with 46% with SPF 15.[25]

Sun-Protection Factor and Application of Sunscreen. Numerous studies have demonstrated that the typical underapplication of sunscreen ranges from 20% to 50% of the recommended 2 mg/cm^2.[26] The exact relationship between SPF and the amount of sunscreen applied, however, is controversial, as some studies of sunscreens with SPF less than 50 have demonstrated an exponential relationship[27,28] whereas other studies with high-SPF sunscreens (≥ 70) have reported a linear relationship.[29,30] Regardless, all studies confirmed that SPF value decreases with inadequate application. This suggests that a high-SPF sunscreen, such as greater than 50, is preferred to compensate for the typical insufficient application of sunscreen.

Caveats. Despite the various advantages of high-SPF products, ultrahigh SPF values such as greater than 70 are more difficult to measure and reproduce during production. In addition, public misinterpretation of higher SPF values as the single most important aspect of photoprotection can lead to a false sense of security. Autier et al showed patients using SPF 30 sunscreen had increased mean cumulative sun exposure and mean duration of sunbathing when compared with the SPF 15 group.[31] Recent FDA-proposed changes to the 2011 FDA sunscreen monograph state that the maximum proposed SPF value on sunscreen labels should be SPF 60 or higher, and sunscreens with an SPF value of 15 or higher should also be required to provide broad-spectrum protection.

Recommendation: A broad-spectrum sunscreen with UVA as well as UVB filters and SPF of at least 30 should be applied, and even-higher SPF sunscreens may be used to compensate for common underapplication of sunscreen. Patients should be educated on the importance of proper application and other important factors affecting effectiveness of sunscreen apart from the SPF value.

Grade of Recommendation: *STRONG*

What is the Preferred Vehicle of Sunscreens? The vehicle of sunscreen is critical for its efficacy and uptake in usage. The formulation of a sunscreen is primarily determined by the emulsifier system.[4] The Mintel global New Products Database shows that, worldwide, emulsion products such as lotions and creams/gel creams are the most popular.[4] Broadly, the emulsion type can be either oil in water (O/W) or water in oil (W/O). In general, the O/W systems are often preferred because of their lighter feel on the skin.[21]

Sohn and colleagues studied in vitro application of sunscreens containing the same filters in different vehicles of W/O, O/W cream, O/W spray, gel, and a clear lipo-alcoholic spray. The W/O resulted in significantly higher SPF than all other formulations. This appears to be due to its more homogenous and thicker film distribution over the applied area.[32] W/O emulsions also have a low hydrophilic-lipophilic balance and use water-insoluble emulsifiers, making them more water-insoluble, thus preventing loss through water contact.[33] The efficacy of an O/W emulsion is diminished as soon as it comes into contact with water.[33] However, as W/O emulsions generally contain more oils than water, they should be avoided on oily skin.[34] Of note, certain W/O formulations with different concentration of filters may absorb oil excess and thus may also have noncomedogenic properties.[34]

Recommendation: The W/O emulsion is the recommended formulation for sunscreens to achieve highest SPF and water resistance. Generally, sunscreens labelled as water resistant with higher SPFs are typically W/O emulsions, whereas those without water-resistant labelling are typically O/W emulsions. However, patient preference for a vehicle with O/W because of its lighter feel and noncomedogenic properties can significantly affect use and therefore may take precedence.

Grade of Recommendation: *WEAK*

Should Inorganic or Organic Sunscreens Be Used? Inorganic (physical) sunscreens were traditionally thicker and whiter formulations, which were not *aesthetically pleasing*. In a small study, most people applied only about 65% of the quantity of inorganic sunscreens compared with organic sunscreens. As a result, the measured SPF of inorganic sunscreens was less than half the organic (chemical) ones.[35] Since the development of micronized particles, many current micronized inorganic sunscreens are much less visible on the skin.[36]

Although media controversy has risen in recent decades regarding systemic absorption of inorganic micronized particles and its potential harms, studies have failed to demonstrate this proposed harm. An in vitro assessment determined that less than 0.03% of a nanoparticulate zinc oxide sunscreen formulation penetrated the uppermost layer of the stratum corneum (SC), and no particles could be detected in the lower SC. These findings were confirmed by 2 studies conducted under in vivo conditions that demonstrated that titanium oxide and zinc oxide nanoparticles were absent or their levels were too low to be tested under the SC, thus making significant penetration toward the underlying keratinocytes unlikely.[37,38] The safety of sunscreens is further detailed in the risk-benefit analysis section of this review.

Recommendation: A broad-spectrum sunscreen containing UVA and UVB filters is recommended, regardless of whether the components are organic or inorganic. When using sunscreens with primarily nonmicronized inorganic filters, it is especially more important to educate the patient regarding adequate application amount since evidence shows underapplication tends to occur.

Grade of Recommendation: *STRONG*

When Should Water-Resistant Sunscreens Be Used? Water-resistant labelling of a sunscreen is determined by how well it binds to skin and withstands adverse conditions such as swimming, sweating, friction, and removal through other physical contact.[36] Currently, Health Canada's 2018 primary sunscreen monograph defines a sunscreen product as either water/sweat resistant for 40 or 80 minutes if it retains protective properties for 40 minutes and 80 minutes, respectively, following moderate activity in 23°C to 32°C (73°F to 90°F) indoor fresh water. Furthermore, "waterproof" or "sweatproof" labels are considered misleading and thus should not be used, reflecting the lack of evidence behind claims of prolonged protection. Stokes and Diffey[39] found that nearly all the protective effect of non–water-resistant products disappeared after 20 minutes of water immersion, and there were no significant differences between SPF retention in "water-resistant" compared with "waterproof" products.

Other than water resistance, friction- or rub-resistant properties could affect the photoprotective effect of sunscreens as well. Stokes and Diffey measured SPF values prior to and after agitation with sand and found that even after allowing 20 minutes for the sunscreen to dry, 15%-60% of the photoprotective effect was lost after contact with the sand.[39]

Recommendation: Water-resistant sunscreen should be worn in conditions where there is significant sweating, water immersion, increased skin friction via physical contact, or contact with sand. Immediate reapplication is necessary to compensate for loss of photoprotective effects after any of these activities.

Grade of Recommendation: *STRONG*

Lip Protection. Lip protection is an important component of safe-sun practice. UVR has been well demonstrated as a risk factor for the development of lip cancers.[40] UV filters are available in many commercial products such as lip balm, lip gloss, and lipstick. Use of photoprotective lip products among female farmers has been correlated to decreased risk of lip cancers.[41]

There are no specific recommendations regarding SPF and application of lip sunscreens from the FDA or Health Canada. When applied to the lip, the SPF value of lipsticks was on average 1.2 units lower than the label SPF of 16.[42] Although this margin between in vitro and in vivo lip application is much smaller compared with sunscreen application on the rest of the body, the authors suggest the practical SPF of lip products must be considered as lower than the manufacturer's label.

Similar to body sunscreens, underapplication of lip sunscreens also occurs. Maier et al showed an application thickness of less than 1 mg/cm^2 for lipsticks during laboratory conditions. In the field experiment in which participants applied lipstick according to their own habits while skiing, the thickness increased to 1.58-1.76 mg/cm^2. This was attributed to increased use in outdoor conditions, where the moisturizing effects of the lipstick encouraged more use. The median daily frequency of application was 2.2-3 times.[43] There are no other data to guide frequency of lip-sunscreen application.

Recommendation: Lip-photoprotective products should be applied generously to cover the whole lip. The use of high-SPF products (≥ 30) and reapplication is empirically recommended to compensate for underapplication.

Grade of Recommendation: *STRONG*

Expiry Date. The literature search yielded no published studies on the effectiveness of sunscreens past the expiry date. Thus, it may be logical to recommend use of sunscreen only within the expiry date to avoid any potential harm, although this is not supported by any evidence. Most sunscreen manufacturers also have a recommended period after opening (POA), which is the maximum duration over which the consumer may use the product after opening. Although the POA for many sunscreens is 12 months, the rationale is unclear. A study has shown that expiry dates relate to the conditions of sunscreen usage, storage, formulation, and form.[44] All sunscreens sold in Canada require an expiry date on the label.[45]

When placed in temperatures ranging from −20°C to 60°C (−4°F to 140°F) for 8 hours, some sunscreens were shown to have phase changes and discolouration at the extremes of temperatures. However, it is unclear whether these macroscopic changes observed would decrease sunscreen efficacy.[46]

Recommendation: Sunscreens should be stored at room temperature to ensure stability. There is a lack of evidence to support whether it is safe or unsafe to use sunscreens past the manufacturers' specified expiry date or recommended PAO.

Grade of Recommendation: *WEAK*

Sunscreen Application

What Amount of Sunscreen Is Appropriate to Apply? The FDA and international protocols recommend applying 2 mg/cm^2 of sunscreen or 35 mL per application to adequately cover 1.73 m^2, the average adult body surface area.[36] This recommendation is well supported by numerous studies.[29,36,47] In particular, a multicentre study[29] found a linear dependence of the SPF on the quantity applied (0.5, 1.0, 2.0 mg/cm^2) and concluded that 2 mg/cm^2 is ideal. However, for the consumer, the 2 mg/cm^2 measurement makes little practical sense. Studies show that consumers typically apply much less, usually between 0.5 and 1.5 mg/cm^2.[31,48] The most important factor in the application of sunscreen is to apply a liberal quantity,[35] and this is the wording used in Canada's updated sun-safety messages.[49] In children, Diaz and colleagues found that application with a controlled device such as a pump or squeeze bottle yielded higher quantity.[50] Ou-Yang et al[30] found sunscreens with SPF 70 and above may compensate for underapplication by consumers.

Recommendation: Sunscreens should be applied liberally to all exposed areas. As a practical estimate to the consumer, approximately 45 ml (the amount of 1 shot glass) would be more than enough to cover the entire body surface of most average-sized individuals, or 2-3 tablespoons for the body and 1-2 teaspoons for the face and neck.[45]

Grade of Recommendation: STRONG

How Frequently Should Sunscreen Be Reapplied? Does Physical Activity Affect the Frequency of Application? Several studies have addressed sunscreen reapplication. Heerfordt showed that double sunscreen application optimizes sunscreen use compared with a single application as the median participant had applied between 13% and 100% more sunscreen at the selected skin sites after double application than single application[51]. In a study of 30 office workers, where half were randomly assigned to having SPF 15-30 sunscreen reapplied after 3 hours, no significant difference in absorption readings (taken at 20 minutes and then hourly for 1-6 hours after initial application) was found in the reapplication group[52]. Similar findings in a split-face design study by Rigel et al.[24] found no difference in erythema with reapplication 2 hours after UV exposure in golfers. Bodekaer et al[53] studied the persistence of sunscreens during physical activity, hot environment, and bathing during an 8-hour period and concluded that one application is sufficient to reduce erythema caused by UVB, although this is assuming the recommended formulation and amount is applied.

To test the recommendation made by many public health agencies to reapply sunscreen every 2-3 hours, Diffey and Grice[35] derived a mathematical model to determine how several factors, including the time of sunscreen reapplication, influence photoprotection. The resultant recommendation is reapplying to exposed sites 15-30 minutes after sun exposure begins and after vigorous activity that could remove sunscreen, such as swimming, toweling, and excessive sweating/rubbing. Reapplying sunscreen during sun exposure is useful to compensate for initial underapplication and replacing sunscreen that may have been removed by water, friction, and/or sweat. Interestingly, SPF 30 sunscreens have been shown to accumulate in the skin when applied 3 times daily, providing a higher SPF.[53] More research is needed to support these findings, however.

An important consideration when applying sunscreen during physical activity is the effect of sweating on sunscreen protection and vice versa. A controlled, randomized, split-face and split-arm clinical study with 24 female participants conducted by Ou-Yang et al[54] found no significant differences in either skin temperatures or sweat rates between the treated (application of sweat-resistant sunscreen) and untreated control skin sites during exercise. As sweating is a crucial process in skin cooling and thermal regulation, this study highlights the safety of using water- or sweat-resistant sunscreen during exercise.

Recommendation: If the appropriate amount of sunscreen is initially applied, reapplication is necessary only after activities that may remove the sunscreen layer, such as swimming, sweating, and friction. There is no clear evidence to suggest a specific frequency of reapplication in the absence of these activities within an 8-hour period.

Grade of Recommendation: STRONG

How Long Before Sun Exposure Should Sunscreen Be Applied? Several review articles state that sunscreen should be applied liberally to exposed sites 15 to 30 minutes prior to sun exposure.[35,36,55] These recommendations are based on how the sunscreens were tested, as there was a complete lack of evidence to support this practice in our literature review. Sunscreen-testing protocols mandate drying times of 15-20 minutes before SPF testing can begin (to ensure water resistance): Mandatory labelling reflects this instruction. There are no data to suggest that there is a delay in sunscreen efficacy; in fact, a recent study showed sunscreen offered immediate protection when applied.[56]

Recommendation: Sunscreen should be applied prior to sun exposure. It would be reasonable to wait 15-30 minutes after application of sunscreen before water exposure to ensure water resistance.

Grade of Recommendation: WEAK

Does Application of Sunscreen Vary for Different Skin Types? Although skin cancer accounts for only 1%-2% of all neoplasms in African Americans and 2%-4% in Asian Americans as compared with 20%-30% of Caucasians, there is a higher morbidity and mortality in individuals of colour as their diagnoses and treatments are often delayed.[36] The average SPF of black skin is 13.4 as compared with white skin, which is 3.4.[57]

A cross-sectional study using the American Cancer Society's sun surveys I and II, a randomized, telephone-based, nationally representative survey of the US population of teens age 11-18 years (n = 1187 in 1998; n = 1931 in 2004)[58] found there was a significant difference between Caucasians and non-Caucasians or Hispanic individuals in their knowledge of the risks of UVR causing cancer and the importance of photoprotection including sunscreen. However, the cosmetic appearance of a tan was significantly less desirable for non-Caucasians or Hispanics than Caucasians.

A cross-sectional study of African American patients (n = 55) attending a primary care medical clinic for dermatological concerns found 74% of respondents had never used sunscreen and that only 15% sunscreen users and 11% nonsunscreen users had ever been counselled to wear sunscreen by either a parent or a medical professional[59]. In contrast, 23% of sunscreen users had experienced a sunburn vs 11% of nonusers had experienced a sunburn, and the majority of all respondents (62% of sunscreen users and 73% of nonsunscreen users) were unaware that African Americans could get skin cancer[59].

A cross-sectional study using the dermatology section of 2003-2006 National Health and Nutrition Examination Survey found that African Americans were 86% less likely than Caucasians to wear sunscreen, and Mexican Americans were 25% less likely to wear sunscreen than Caucasians. Of all the participants who reported having a severe sunburn, African Americans had a 7-fold lower likelihood of wearing sunscreen than their white counterparts.[4]

Currently, there are no studies that assess the absolute risk reduction of sunscreen use and skin cancer in people of colour (African, Asian, or Latino descent). There is a need to quantify this risk reduction as 1 in 5 Canadians identified as visible minorities in 2011[60].

Recommendation: People of colour tend to underuse photoprotection, including sunscreen. More data are needed to understand the risk reduction provided by sunscreen, beyond just sunburn.

Grade of Recommendation: WEAK

Risk-Benefit Analysis

Is Sunscreen Harmful (ie, Risks of Compounds/Ingredients)? There has been lots of media attention surrounding the potential harmful health effects of sunscreen. Recently the FDA issued a new amendment to its sunscreen monograph and changes to its designation of ingredients labelled as "generally recognized as safe and effective" (GRASE). Although there are no urgent safety concerns, more safety and efficacy data on 12 organic (chemical) sunscreen ingredients (cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, padimate O, sulisobenzone, oxybenzone, and avobenzone) are required before sunscreens with those ingredients can be labelled as GRASE. These compounds have not been deemed unsafe, but it is felt more information is needed. Currently, the inorganic (physical) filters titanium dioxide and zinc oxide are considered GRASE for use in sunscreens, whereas PABA and trolamine salicylate are not GRASE because of safety issues.

As mentioned in the inorganic vs. organic section above, concerns regarding the potential systemic absorption of nanoparticles found in physical sunscreen formulations have been alleviated by studies showing lack of absorption through the stratum corneum.[37,38]

Components in chemical sunscreens have been implicated in photoallergic contact dermatitis, particularly benzophenone-3, octyl methoxycinnamate, and octocrylene.[61,62] Similarly, a review found that although allergy to sunscreen represents a small proportion (<1%) of allergic contact dermatitis reactions in North America, it is one of the most common causes of photoallergy63. On the other hand, a meta-analysis[64] of 64 exaggerated-use studies found that sunscreen products formulated with 1%-6% oxybenzone do not possess a significant sensitization or irritation potential for the general public and that the incidence rate is actually overestimated in the literature.

Concern has also been raised regarding benzophenone UVR filters and their reported estrogenic and antiandrogenic activity. A prospective cohort study[65] found that male exposure to select UV filters (BP-2 and 4-hydroxybenzophenone) may diminish couples' fecundity, resulting in a longer time to pregnancy. In another study by Janjua[66], although oxybenzone (also known as BP-3) and octinoxate were systemically absorbed after 1 week's application, no significant change in reproductive hormone levels was detected. However, a recent systematic review[67] suggests exposure to BP-3 is statistically associated with reproductive toxicity in humans and animals, but the clinical significance is unclear. In human studies, high levels of BP-3 exposure were shown to be linked to an increase in male birth weight but a decline in female birth weight and male gestational age, but not other reproductive outcomes, including semen motility, female fecundity, male idiopathic infertility, spontaneous abortion, male genital abnormalities, and reproductive hormone levels. Animal studies, however, demonstrated negative reproductive outcomes including decreased egg production, hatching, testosterone, and epididymal sperm density as well as prolonged estrous cycles. The prevalence of total exposure to BP-3 by the general public is high, as phenolic compounds like BP-3 are prevalent in the air, drinking water, food, and personal care products.[68] Although the safety threshold of BP-3 exposure is unclear, studies report a systematic absorption of BP-3 in humans at a rate of up to 2% after dermal application. Oxybenzone is used in a variety of other products, such as plastics as a photostabilizer, and cosmetic products, including shampoo, cream, lotion, hairspray, nail polish, and perfume. Overall, no consensus appears to exist regarding the estrogenic and antiandrogenic activity of UV filters and the clinical relevance remains uncertain.

In addition, environmental concerns about some UV filters have been raised. An in vitro study demonstrated that BP-3 may pose a hazard to coral reefs and their resiliency to climate change as it produces morphological deformities, damages their DNA, and acts as an endocrine disruptor.[69] Similarly, a review showed that BP-3 may be a contributor to coral reef bleaching, although the role of warming ocean temperatures and pollutants is a strong confounder.[70] Furthermore, they found the presence of organic UV filters in almost all water sources and various fish species worldwide, and that these UV filters are not easily removed by common wastewater treatment-plant technique. The current concentration these agents in the water is not at a toxic level for coral reefs, but these important signals require further study, as these concentrations may rise in the future with BP-3 and other filters in so many daily-use products.

Recommendation: There are no definitive data to support that sunscreen filters cause any toxicity in humans. There are some signals that there is a need for further study on the effect of certain UV filters on the environment. The SC appears to be an effective barrier against the penetration of inorganic zinc and titanium dioxide nanoparticulates; therefore, significant systemic absorption should not be a concern. The most common adverse effect of using chemical sunscreens is the risk of photoallergy, and overall the prevalence is quite low. There is currently a lack of evidence to suggest sunscreens containing benzophenone filters lead to decreased fertility. Although a recent laboratory study suggests oxybenzone may pose a hazard to coral, more research is needed, particularly because a direct association between sunscreen posing a threat has not been established, especially given its abundance in various other products.

Grade of Recommendation: STRONG

Are Sunscreens Safe for Infants? Health Canada recommends sunscreen use for children older than age 6 months and to consult a health care practitioner regarding its use in younger children (Health Canada 2015). Avoidance of sun and protective clothing are the mainstay for sun safety in infants younger than age 6 months. The CDA, the Canadian Pediatrics Society (CPS), and the American Academy of Pediatrics (AAP) state that sunscreen can be applied to small areas that clothing cannot cover such as the face or back of the hands (CDA 2016, CPS 2011, AAP 2015), but should be washed off when sun protection is no longer needed. The CDA and the CPS recommend using a sunscreen with an SPF of 30, whereas the AAP recommends sunscreen with an SPF of 15 or greater. There are no studies that directly evaluate the safety of sunscreens in infants younger than age 6 months. Young infants have a higher body surface-to-mass ratio and absorptive area in combination with their underdeveloped skin, including a thinner SC and epidermal thickness and lower lipid-to-protein ratio, allowing for more sunscreen to be potentially absorbed.[71] In particular, newer sunscreens contain nanoparticles, and this risk has not been quantified for infants who have thinner SCs than adults.[37] A cohort study of 54 pairs of mothers and babies found UV filters were present in 85% of breast milk samples, only 55% of women reporting using sunscreens[72], suggesting that some women are exposed to UV filters in their other cosmetic products or there is potentially recall bias. The health implication of these UV filters in breast milk requires further elucidation.

Recommendation: There is a lack of evidence examining the pharmacokinetics of sunscreens in young infants that contributes to recommendations based largely on theoretical harm vs empirical data. Clinical trials in this vulnerable age group are very difficult to design to meet today's ethical standards. It is reasonable given the paucity of evidence to continue to limit the use of sunscreen in children younger than age 6 months as physiologically their skin is immature and there are theoretically potential risks of nanoparticles and UV filters being absorbed. Photoprotection should be based largely on behavioural modification in this group, such as avoiding peak UV hours, seeking shade, and using protective clothing.

Grade of Recommendation: WEAK

Does Sunscreen Prevent Skin Damage/Aging/Wrinkles? Cumulative UV exposure is a major contributing factor in aging skin. Regular use of sunscreen protects against signs of photoaging, including rhytides, pigmentary changes, and telangiectasias.

From biopsy-specimen analysis, Phillips and colleagues concluded that daily use of sunscreen reduces UV exposure-related skin damage compared with intermittent use of equal or higher SPF products.[73] Similarly, Seité demonstrated that daily moisturizers with broad-spectrum sunscreen protected against solar UV-induced skin damages in the epidermis and dermis and daily application prevents UVA radiation-induced transcriptional expression of genes that are directly linked to skin aging and also reflect the skin's antioxidative stress defense response.[74]

A photostable sunscreen with SPF 55 and high UVA protective factor provided proportionately high protection against multiple cellular damage markers known to contribute to photoaging.[75] Meinke et al found that sunscreens even offer protection in the infrared spectrum, which, as in the UV-wavelength range, also generates free radicals, contributing to photoaging.[76]

Hughes et al[77] published the results of a pivotal randomized controlled trial. A total of 903 adult Australians were randomized to daily use or discretionary use of sunscreen (control). The daily sunscreen group showed no detectable increase in skin aging after 4.5 years; skin aging from baseline to the end of the trial was 24% less in the daily sunscreen group than in the discretionary sunscreen group. In fact, a systematic review of randomized controlled trials shows that evidence, though limited, supports beneficial effects of sunscreen application on photoaging.[78] Similarly, another review of clinical trials demonstrates that sunscreens containing Ecamsule (Mexoryl SX), a widely used chemical sunscreen filter, prevent the impact of UVA on skin photodamage.[79]

Recommendation: There is strong evidence in the literature, including results from randomized controlled trials, that sunscreen prevents photoaging.

Grade of Recommendation: STRONG

Does Sunscreen Prevent Skin Cancer? A randomized controlled trial of adult Australians[80] found that after prolonged follow-up, squamous cell carcinoma tumour rates were decreased by almost 40% in people randomized to daily sunscreen use compared with those with discretionary use. Basal cell carcinoma tumour rates tended to decrease as well, but not significantly. Another randomized controlled trial found daily use of sunscreen prevents and/or retards the development of solar keratoses among adults.[81] Moreover, regular use of sunscreen has been shown to be cost effective in NMSC and actinic keratosis prevention.[82] Ten years after the Australian randomized controlled trial cessation, 11 new primary melanomas were identified in the daily sunscreen group and 22 in the discretionary group, showing that melanoma may also be preventable by regular sunscreen use in adults.[83]

Conflicting data presented in a systematic review and meta-analysis[84] showed no association between sunscreen use and risk of melanoma and NMSC in the general population. However, this review, which included 28 observational studies and only 1 community-based randomized trial, had major limitations. First, many of the included case-control trials used primarily UVB sunscreens rather than broad-spectrum filters. Second, only 5 of the included studies addressed NMSC. Although it is plausible that the benefit of sunscreen use in melanoma development may vary, because of its multifactorial nature, which includes multiple genetic factors, squamous and basal cell carcinoma have been shown to be more strongly linked to sun exposure.[85] Third, there was a low quality of evidence overall due to inconsistencies among included studies and its retrospective design. Rueegg et al found heterogeneous summary estimates for the sunscreen-melanoma association from observational studies but a protective effect of sunscreen against skin cancer in the only randomized controlled trial performed.[86]

Recommendation: Regular sunscreen use can prevent melanoma and NMSC. The literature that suggests there is no effect of sunscreen on the development of skin cancer is flawed in that it does not take well-established skin cancer risk factors into account.

Grade of Recommendation: *STRONG*

Discussion

Sunscreens are widely used; however, some widely promoted sun-safety messages do not reflect current evidence. In this review, we have evaluated and discussed the strength of recommendations relating to the efficacy of physical barriers, sunscreen properties and application, and risk-benefit analysis.

Our review of 18 years of literature yielded an overall lack of high-quality evidence. A total of 84 studies were included in this review addressing 16 questions that described the physical barriers, sunscreen properties and application, and risk-benefit analysis. There is strong evidence supporting the use of a broad-spectrum UVA and UVB sunscreen with a minimum SPF of 30, applied liberally to all exposure areas including the lips. Higher SPF is recommended, reapplication may be considered to compensate for underapplication but is not mandatory, and water-resistant sunscreen is recommended for physical activity. There is strong evidence supporting the safety profile of sunscreens and their efficacy in photoaging and melanoma and NMSC prevention.

There are several limitations to this review. First, the recommendations that were graded as weak had a high degree of heterogeneity or limited data in the existing evidence. There was weak evidence supporting the use of photoprotection in children younger than age 6 months, although the evidence is expected to be inherently weaker as there is a lack of studies for ethical reasons. The use of photoprotective clothing and sunglasses, the importance of the sunscreen expiry date, the use of sunscreen in people of colour, and the potential environmental and reproductive toxicity of sunscreens are supported by weak evidence because of the limited number of studies. Second, this review included studies published only in English, which presents language bias and may limit the analysis of some research questions. The inclusion of non-English studies may allow for a greater ability to answer some research questions or to further increase the strength of some recommendations presented in this review. Despite these limitations, the existing body of evidence suggests sunscreen is one of the best-supported photodamage-prevention options, especially given the relatively high risk of photodamage and skin cancer associated with UV exposure.

This in-depth review consolidates the available evidence supporting sun-protection guidelines. The 2016 National Consensus study on the Recommended Core Content for Sun Safety Messaging for public education in Canada was the most recent up-to-date source of information for clinicians since its last update in 1945. This current review adds more up-to-date information and an in-depth analysis of the evidence to the 2016 consensus study. Clinicians should be aware of the strength of evidence when making routine recommendations on sunscreen use. This is particularly important when considering that skin cancer is the most common cancer in Canada and is largely preventable.[3]

Conclusion

Our review revealed that the level of evidence supporting recommendations for the use of sunscreens and other sun-protection methods varies from fair to good, as assessed using the CTFPHC's GRADE system. Our updated recommendations, derived from a critical appraisal of the literature, are a useful educational tool for the practicing dermatologist in counselling patients about sun safety.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Supplemental Material

Supplemental material for this article is available online.

ORCID iD

Heidi Li https://orcid.org/0000-0001-6495-088X

References

1. Canadian Cancer Society. *Canadian Cancer Statistics 2014: special topic: skin cancers*. 2014. http://www.cancer.ca/~/media/cancer.ca/CW/cancerinformation/cancer101

/Canadiancancerstatistics/Canadian-Cancer-Statistics-2014-EN.pdf. Accessed December 12, 2018.
2. Krueger H, Williams D, Chomiak M, Trenaman L. *The Economic Burden of Skin Cancer in Canada: Current and Projected*. 2010. http://krueger.ca/wp-content/uploads/2015/08/skincancer.pdf. Accessed December 12, 2018.
3. Armstrong BK, Kricker A. The epidemiology of UV induced skin cancer. *J Photochem Photobiol B Biol*. 2001;63(1-3):8-18. doi:10.1016/S1011-1344(01)00198-1
4. Kullavanijaya P, Lim HW. Photoprotection. *J Am Acad Dermatol*. 2005;52(6):937-958. doi:10.1016/j.jaad.2004.07.063
5. Marrett LD, Chu MB, Atkinson J, et al. An update to the recommended core content for sun safety messages for public education in Canada: a consensus report. *Can J Public Health*. 2016;107(4-5):e473-e479. doi:10.17269/CJPH.107.5556
6. Bell N, Connor Gorber S, Tonelli M, et al. From ABCs to GRADE: Canadian Task Force on Preventive Health Care's new rating system for clinical practice guidelines. *Can Fam Physician*. 2013;59(12):1282-1289.
7. Wang SQ Lim HW, eds. *Principles and Practice of Photoprotection*. Switzerland: Springer International Publishing; 2016.
8. Government of Canada. Consumer guidance on UV protective clothing. https://www.competitionbureau.gc.ca/eic/site/cb-bc.nsf/eng/02391.html. 2007. Accessed December 12, 2018
9. Gies P. Photoprotection by clothing. *Photodermatol Photoimmunol Photomed*. 2007;23:264-274. doi:10.1111/j.1600-0781.2007.00309.x
10. Sarkar AK. An evaluation of UV protection imparted by cotton fabrics dyed with natural colorants. *BMC Dermatol*. 2004;4(1):15. doi:10.1186/1471-5945-4-15
11. Crews P., Kachman S. BA. No title. *Text Chem Color*. 1999;31(6):17-26. doi:10.3403/00776353
12. Wright AL, Hart GC, Peirce SC. Clothing protection factor of a replica England football shirt. *Lancet*. 1998;351(9117):1706. doi:10.1016/S0140-6736(05)77745
13. Gambichler T, Rotterdam S, Altmeyer P, Hoffmann K. Protection against ultraviolet radiation by commercial summer clothing: need for standardised testing and labelling. *BMC Dermatol*. 2001;1:6. doi:10.1186/1471-5945-1-6
14. Ghazi S, Couteau C, Coiffard LJM. How to guarantee adequate sun protection for a young sportsperson. 2011;2011(Band 9):470-474. doi:10.1111/j.1610-0387.2011.07660.x
15. Moehrle M, Garbe C. Solar UV-Protective Properties of Textiles. *Dermatology*. 2000;201(1):82. doi:10.1159/000018444
16. Bielinski K, Bielinski N. UV Radiation transmittance: Regular clothing versus sun-protective clothing. *Cutis*. 2014;94(September):135-138.
17. Dain SJ, Phuong T, Ngo T, et al. Sunglasses , the European directive and the European standard. 2010:253-256. doi:10.1111/j.1475-1313.2010.00711.x
18. Tuchinda C, Srivannaboon S, Lim HW. Photoprotection by window glass, automobile glass, and sunglasses. *J Am Acad Dermatol*. 2006;54(5):845-854. doi:10.1016/j.jaad.2005.11.1082
19. Sliney DH. Photoprotection of the eye – UV radiation and sunglasses. 2001;64:166-175.
20. Behaviors KS, Pichon LC, Mayer JA, et al. Ethnoracial Differences Among Outdoor Workers in. 2005;28(4). doi:10.1016/j.amepre.2005.01.004
21. Osterwalder U, Sohn M, Herzog B. Global state of sunscreens. *Photodermatol Photoimmunol Photomed*. 2014;30(2-3):62-80. doi:10.1111/phpp.12112
22. Reinau D, Weiss M, Meier CR, Diepgen TL, Surber C. Outdoor workers ' sun-related knowledge , attitudes and protective behaviours : a systematic review of cross- sectional and interventional studies. 2013;(Cmm). doi:10.1111/bjd.12160
23. Williams JD, Maitra P, Atillasoy E, Wu M-M, 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;78(5):902-910.e2. doi:10.1016/j.jaad.2017.12.062
24. Russak JE, Chen T, Appa Y, Rigel DS. A comparison of sunburn protection of high–sun protection factor (SPF) sunscreens: SPF 85 sunscreen is significantly more protective than SPF 50. *J Am Acad Dermatol*. 2010;62(2):348-349. doi:10.1016/j.jaad.2009.05.025
25. Pissavini M, Diffey B. The likelihood of sunburn in sunscreen users is disproportionate to the SPF. *Photodermatol Photoimmunol Photomed*. 2013;29(3):111-115. doi:10.1111/phpp.12033
26. Petersen B, Wulf HC. Application of sunscreen − theory and reality. *Photodermatol Photoimmunol Photomed*. 2014;30(2-3):96-101. doi:10.1111/phpp.12099
27. Couteau C, Paparis E, El-Bourry-Alami S, Coiffard LJ. Influence on SPF of the quantity of sunscreen product applied. *Int J Pharm*. 2012;437(1-2):250-252. doi:10.1016/j.ijpharm.2012.08.019
28. Faurschou A, Wulf HC. The relation between sun protection factor and amount of sunscreen applied in vivo. *Br J Dermatol*. 2007;156(4):716-719. doi:10.1111/j.1365-2133.2006.07684.x
29. Bimczok R, Gers-Barlag H, Mundt C, et al. Influence of applied quantity of sunscreen products on the sun protection factor – a multicenter study organized by the DGK Task Force Sun Protection. *Skin Pharmacol Physiol*. 2007;20(1):57-64. doi:10.1159/000096173
30. Ou-Yang H, Stanfield J, Cole C, Appa Y, Rigel D. High-SPF sunscreens (SPF $\geq$70) may provide ultraviolet protection above minimal recommended levels by adequately compensating for lower sunscreen user application amounts. *J Am Acad Dermatol*. 2012;67(6):1220-1227. doi:10.1016/j.jaad.2012.02.029
31. Autier P, Doré JF, Négrier S, et al. Sunscreen use and duration of sun exposure: a double-blind, randomized trial. *J Natl Cancer Inst*. 1999;91(15):1304-1309. doi:10.1093/jnci/91.15.1304
32. Sohn M, Hêche A, Herzog B, Imanidis G. Film thickness frequency distribution of different vehicles determines sunscreen efficacy. *J Biomed Opt*. 2014;19(11):115005. doi:10.1117/1.JBO.19.11.115005
33. Couteau C, Demé A, Cheignon C, Coiffard LJ. Influence of the hydrophilic-lipophilic balance of sunscreen emulsions on their water resistance property. *Drug Dev Ind Pharm*. 2012;38(11):1405-1407. doi:10.3109/03639045.2011.653362
34. Lott D, Lewellen K, Wiener G. High sunscreen efficiency water-in-oil emulsion. http://www.freepatentsonline.com/7790146.html. Accessed April 3, 2019.
35. Diffey BL, Grice J. The influence of sunscreen type on photoprotection. *Br J Dermatol*. 1997;137(1):103-105. doi:10.1046/j.1365-2133.1997.17761863.x

36. Moloney FJ, Collins S, Murphy GM. Sunscreens: safety, efficacy and appropriate use. *Am J Clin Dermatol*. 2002;3(3):185-191. doi:10.2165/00128071-200203030-00005
37. Mohammed YH, Holmes A, Haridass I, et al. Support for the safe use of zinc oxide nanoparticle sunscreens: lack of skin penetration or cellular toxicity after repeated application in volunteers. *J Invest Dermatol*. 2019;139(2):308-315. doi:10.1016/j.jid.2018.08.024
38. Filipe P, Silva JN, Silva R, et al. Stratum corneum is an effective barrier to TiO_2 and ZnO nanoparticle percutaneous absorption. *Skin Pharmacol Physiol*. 2009;22(5):266-275. doi:10.1159/000235554
39. Stokes RP, Diffey BL. A novel ex vivo technique to assess the sand/rub resistance of sunscreen products. *Int J Cosmet Sci*. 2000;22(5):329-334. doi:10.1046/j.1467-2494.2000.00027.x
40. Gallagher RP, Lee TK, Bajdik CD, Borugian M. Ultraviolet radiation. *Chronic Dis Can*. 2010;29(suppl 1):51-68.
41. Pogoda JM, Preston-Martin S. Solar radiation, lip protection, and lip cancer risk in Los Angeles County women (California, United States). *Cancer Causes Control*. 1996;7(4):458-463. doi:10.1007/BF00052672
42. Gabard B, Ademola J. Lip sun protection factor of a lipstick sunscreen. *Dermatology*. 2001;203(3):244-247. doi:10.1159/000051758
43. Maier H, Schauberger G, Brunnhofer K, Hönigsmann H. Assessment of thickness of photoprotective lipsticks and frequency of reapplication: results from a laboratory test and a field experiment. *Br J Dermatol*. 2003;148(4):763-769. doi:10.1046/j.1365-2133.2003.05032.x
44. Gagliardi L, Bonadonna L, Brianeesco R, et al. A study on sunscreen products: determination of PaO (period after opening) [article in Italian]. *Rivista Italiana Delle Sostanze Grasse*. 2008;85(2):107-119.
45. Health Products and Food Branch. *Primary Sunscreen Monograph*. 2018:1-15. http://webprod.hc-sc.gc.ca/nhpid-bdipsn/atReq.do?atid=sunscreen-ecransolaire&. Revised December 7, 2018. Accessed January 13, 2019.
46. Jung GW, Ting PT, Salopek TG. Stability of sunscreens and sunblocks following exposure to extreme temperatures. *J Am Acad Dermatol*. 2012;66(6):1007-1009. doi:10.1016/j.jaad.2011.10.010
47. Schalka S, dos Reis VM, Cucé LC. The influence of the amount of sunscreen applied and its sun protection factor (SPF): evaluation of two sunscreens including the same ingredients at different concentrations. *Photodermatol Photoimmunol Photomed*. 2009;25(4):175-180. doi:10.1111/j.1600-0781.2009.00408.x
48. Autier P, Doré JF, Cattaruzza MS, et al. Sunscreen use, wearing clothes, and number of nevi in 6- to 7-year-old European children. European Organization for Research and Treatment of Cancer Melanoma Cooperative Group. *J Natl Cancer Inst*. 1998;90(24):1873-1880. doi:10.1093/jnci/90.24.1873
49. Marrett LD, Chu MB, Atkinson J, Rosen CF. An update to the recommended core content for sun safety messgaes for public education in Canada: A consensus report.
50. Diaz A, Neale RE, Kimlin MG, Jones L, Janda M. The Children and Sunscreen Study: a crossover trial investigating children's sunscreen application thickness and the influence of age and dispenser type. *Arch Dermatol*. 2012;148(5):606-612. doi:10.1001/archdermatol.2011.2586
51. Heerfordt IM, Torsnes LR, Philipsen PA, Wulf HC. Sunscreen use optimized by two consecutive applications. 2018:1-11.
52. Elliott T, Nehl EJ, Glanz K. A controlled trial of objective measures of sunscreen and moisturizing lotion. *Cancer Epidemiol Biomarkers Prev*. 2009;18(5):1399-1402. doi:10.1158/1055-9965.EPI-08-0492
53. Bodekær M, Åkerström U, Wulf HC. Accumulation of sunscreen in human skin after daily applications: a study of sunscreens with different ultraviolet radiation filters. *Photodermatol Photoimmunol Photomed*. 2012;28(3):127-132. doi:10.1111/j.1600-0781.2012.00651.x
54. Ou-Yang H, Meyer K, Houser T, Grove G. Sunscreen formulations do not interfere with sweat cooling during exercise. *Int J Cosmet Sci*. 2018;40(1):87-92. doi:10.1111/ics.12440
55. Sambandan DR, Ratner D. Sunscreens: an overview and update. *J Am Acad Dermatol*. 2011;64(4):748-758. doi:10.1016/j.jaad.2010.01.005
56. de Gálvez MV, Aguilera J, Buendía EA, Sánchez-Roldán C, Herrera-Ceballos E. Time required for a standard sunscreen to become effective following application: a UV photography study. *J Eur Acad Dermatology Venereol*. 2018;32(4):e123-e124. doi:10.1111/jdv.14626
57. Sayre RM, Dowdy JC, Lott DL, Marlowe E. Commentary on 'UVB-SPF': the SPF labels of sunscreen products convey more than just UVB protection. *Photodermatol Photoimmunol Photomed*. 2008;24(4):218-220. doi:10.1111/j.1600-0781.2008.00360.x
58. Bandi P, Cokkinides VE, Weinstock MA, Ward E. Sunburns, Sun protection and indoor tanning behaviors, and attitudes regarding sun protection benefits and tan appeal among parents of U.S. adolescents—1998 compared to 2004. *Pediatr Dermatol*. 2010;27(1):9-18. doi:10.1111/j.1525-1470.2009.01074.x
59. J Briley J, L Lynfield Y, Chavda K. *Sunscreen Use and Usefulness in African-Americans*. Vol 6.; 2007.
60. Statistics Canada. National Household Survey. *Immigr Ethnocult Divers Canada*. 2013;99-010-X20(99):1-23. doi:99-010-X2011001
61. Rodríguez E, Valbuena MC, Rey M, Porras de Quintana L. Causal agents of photoallergic contact dermatitis diagnosed in the national institute of dermatology of Colombia. *Photodermatol Photoimmunol Photomed*. 2006;22(4):189-192. doi:10.1111/j.1600-0781.2006.00212.x
62. Avenel-Audran M, Dutartre H, Goossens A, et al. Octocrylene, an emerging photoallergen. *Arch Dermatol*. 2010;146(7):753-757. doi:10.1001/archdermatol.2010.132
63. Goossens A. Photoallergic contact dermatitis. *Photodermatol Photoimmunol Photomed*. 2004;20(3):121-125. doi:10.1111/j.1600-0781.2004.00092.x
64. 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;24(4):211-217. doi:10.1111/j.1600-0781.2008.00363.x
65. Buck Louis GM, Kannan K, Sapra KJ, Maisog J, Sundaram R. Urinary concentrations of benzophenone-type ultraviolet radiation filters and couples' fecundity. *Am J Epidemiol*. 2014;180(12):1168-1175. doi:10.1093/aje/kwu285
66. Janjua NR, Mogensen B, Andersson A-M, et al. 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;123(1): 57-61. doi:https://doi.org/10.1111/j.0022-202X.2004.22725.x
67. 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;73: 175-183. doi:10.1016/j.reprotox.2017.08.015
68. Centers for Disease Control and Prevention (CDC). THMs-DBP FactSheet. Fourth National Report on Human Exposure to Environmental Chemicals (Fourth Report). 2004;3. https://www.cdc.gov/biomonitoring/pdf/FourthReport_UpdatedTables_Feb2015.pdf. Revised February 2015. Accessed January 13,
69. Downs CA, Kramarsky-Winter E, Segal R, et al. 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;70(2):265-288. doi:10.1007/s00244-015-0227-7
70. Schneider SL, Lim HW. Review of environmental effects of oxybenzone and other sunscreen active ingredients. *J Am Acad Dermatol.* 2019;80(1):266-271. doi:10.1016/j.jaad.2018.06.033
71. Blume-Peytavi U, Tan J, Tennstedt D, et al. Fragility of epidermis in newborns, children and adolescents. *J Eur Acad Dermatology Venereol*. 2016;30:3-56. doi:10.1111/jdv.13636
72. Schlumpf M, Durrer S, Faass O, et al. Developmental toxicity of UV filters and environmental exposure: A review. *Int J Androl*. 2008;31(2):144-151. doi:10.1111/j.1365-2605.2007.00856.x
73. Phillips TJ, Bhawan J, Yaar M, Bello Y, LoPiccolo D, Nash JF. Effect of daily versus intermittent sunscreen application on solar simulated UV radiation–induced skin response in humans. *J Am Acad Dermatol*. 2000;43(4):610-618. doi:10.1067/mjd.2000.107244
74. Seité S, Reinhold K, Jaenicke T, Brenden H, Krutmann J, Grether-Beck S. Broad-spectrum moisturizer effectively prevents molecular reactions to UVA radiation. *Cutis*. 2012;90(6):321-326. http://europepmc.org/abstract/MED/23409485.
75. Cole C, Appa Y, Ou-Yang H. A broad spectrum high-SPF photostable sunscreen with a high UVA-PF can protect against cellular damage at high UV exposure doses. *Photodermatol Photoimmunol Photomed*. 2014;30(4):212-219. doi:10.1111/phpp.12124
76. Meinke MC, Haag SF, Schanzer S, Groth N, Gersonde I, Lademann J. Radical protection by sunscreens in the infrared spectral range. *Photochem Photobiol*. 2011;87(2):452-456. doi:10.1111/j.1751-1097.2010.00838.x
77. Hughes MCB, Williams GM, Baker P, Green AC. Sunscreen and prevention of skin aging: A randomized trial. *Ann Intern Med*. 2013;158(11):781-790. doi:10.7326/0003-4819-158-11-201306040-00002
78. Iannacone MR, Hughes MCB, Green AC. Effects of sunscreen on skin cancer and photoaging. *Photodermatol Photoimmunol Photomed*. 2014;30(2-3):55-61. doi:10.1111/phpp.12109
79. Séite S, Moyal D, Richard S, et al. Mexoryl® SX: a broad absorption UVA filter protects human skin from the effects of repeated suberythemal doses of UVA. *J Photochem Photobiol B Biol*. 1998;44(1):69-76. doi:10.1016/S1011-1344(98)00122-5
80. 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;15(12):2546 LP - 2548. doi:10.1158/1055-9965.EPI-06-0352
81. Darlington S, Williams G, Neale R, Frost C, Green A. A randomized controlled trial to assess sunscreen application and beta carotene supplementation in the prevention of solar keratoses. *JAMA Dermatology*. 2003;139(4):451-455. doi:10.1001/archderm.139.4.451
82. Hirst NG, Gordon LG, Scuffham PA, Green AC. Lifetime cost-effectiveness of skin cancer prevention through promotion of daily sunscreen use. *Value Heal*. 2012;15(2):261-268. doi:10.1016/j.jval.2011.10.009
83. Green A, Siskind V, Bain C, Alexander J. Sunburn and malignant melanoma. *Br J Cancer*. 1985;51(3):393-397. doi:10.1038/bjc.1985.53
84. Silva ES da, Tavares R, Paulitsch F da S, Zhang L. Use of sunscreen and risk of melanoma and non-melanoma skin cancer: A systematic review and meta-analysis. *Eur J Dermatol*. 2018;28(2):186-201. doi:10.1684/ejd.2018.3251
85. Savoye I, Olsen CM, Whiteman DC, et al. Patterns of ultraviolet radiation exposure and skin cancer risk: The E3N-SunExp study. *J Epidemiol*. 2018;28(1):27-33. doi:10.2188/jea.JE20160166
86. Rueegg CS, Stenehjem JS, Egger M, et al. Challenges in assessing the sunscreen-melanoma association. *Int J Cancer*. 2018. doi:10.1002/ijc.31997