Research Review
EDUCATIONAL SERIES

An Update on Sunscreens III

This review updates recent research on the epidemiology of skin cancer and the associated risk factors as well as the role of sunscreen use in the prevention of skin cancer, including adherence issues and controversies surrounding its use. Louise Reiche (Palmerston North) and Craig Sinclair (Melbourne) provide expert comment and recommendations. This review is intended as an educational resource for healthcare professionals.

About the Commentators

Dr Louise Reiche
MBChB (Otago), FRACP, FNZDS, MD

Dr Louise Reiche is a New Zealand physician trained vocational specialist dermatologist. Experienced in a wide range of general clinical dermatology, she sees the impact of NZ sun exposure on her patients on a daily basis and pleasing results from sun protection interventions.

Louise has served on the Vitamin D Working Group for the Cancer Society, is a member of Melnet NZ, and works alongside these groups and on behalf of the NZ Dermatological Society promoting varied sun protection practices in an expert voluntary capacity.

Craig Sinclair
Director, Cancer Prevention Centre, Cancer Council Victoria

Craig Sinclair is one of Australia's leading experts on skin cancer prevention.

Mr Sinclair heads the World Health Organization's (WHO) Collaborative Centre for UV Radiation and has particular expertise in skin cancer, vitamin D and sun protection.

As chair of Cancer Council Australia's Public Health Committee and Director of the Cancer Prevention Centre at Cancer Council Victoria, Mr Sinclair is also an expert media commentator on a broad range of public health issues related to cancer prevention and screening. Mr Sinclair has provided advice to health authorities in Australia and internationally on public health issues, including the UK Home Office and Health Education Authority, the Canadian Cancer Society and the WHO.

He is an author of a number of WHO publications including the Risks and Guidance on Artificial Tanning Sunbeds and the Local Authorities Guide on UV Radiation and Health. As the Director of the WHO Collaborative Centre for UV Radiation, Craig is a regular advisor to the WHO in the area of UV Radiation.

In 2010, the United States Environment Protection Agency (EPA) awarded Craig with an EPA Montreal Protocol Award for his substantial contribution to human health protection.

Epidemiology of Skin Cancer

Melanoma and non-melanoma skin cancer are now the most common types of cancer in light-skinned populations.[1] In 2010, melanoma incidence and mortality rates were 39.8 per 100,000 and 5.0 per 100,000 people in New Zealand, respectively, and 49.4 per 100,000 and 6.3 per 100,000 people in Australia.[2,3] These rates, both incidence and mortality, are the highest in the world and are consistent with New Zealand and Australia having high levels of ambient ultraviolet radiation (UV).[4]

Melanoma rates have been relatively stable in both New Zealand and Australia over the past 10 years.[5] In terms of melanoma mortality, however, trends in New Zealand and Australia differ.[4] Although mortality rates for both genders in Australia and New Zealand have increased over the past 40 years, the increase has been greater in New Zealanders and in women especially. This may be due to a delayed response to melanoma prevention activities compared with Australia.[4] The data also indicate a significant reduction in melanoma mortality rates in younger men and women (15-44 years of age) in Australia,[4] which is likely due to skin cancer prevention campaigns having an effect. The age-related picture in New Zealand is more complicated with only younger women showing a significant reduction in melanoma mortality.[4]

Although improvements in mortality have been observed in some groups, the overall epidemiological data set indicates the need for continued skin cancer prevention efforts in both Australia and New Zealand.

Early-life UV Exposure and Skin Cancer Risk

The main modifiable risk factor for non-melanoma and melanoma skin cancers is exposure of the skin to UV, with the total dose received largely determined by ambient UV levels and patterns of personal behaviour.[4,6]

Recent research from the US suggests that sun exposure in early life and adulthood is predictive of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) risks, whereas melanoma risk is mainly associated with sun exposure in early life.[7] Twenty-year follow-up data from the 1989–2009 Nurses' Health Study II were analysed to assess the relative contributions of skin cancer risk factors to the development of skin cancer. After controlling for other risk factors, cumulative UV exposure in both children and adults was found to be significantly associated with increased risk for developing BCC and SCC, but not melanoma. However, the number of blistering sunburns between ages 15 and 20 years was strongly associated with increased melanoma risk.[7] These results demonstrate that prevention of skin cancer, especially melanoma, begins in childhood via the avoidance of UV exposure. Hence, parents should be advised to pay more attention to protecting their children from early-life sun exposure to reduce their risk of melanoma later in life.

Healthcare professionals need to be aware, however, that UV exposure in adult life is still relevant to melanoma mortality and to continue to provide sun protection advice when the Sun Protection Alert (see page 3) is displayed.

A review of studies that assessed the effectiveness of interventions aimed at modifying sun exposure behaviour in children in the US, Australia and Europe concluded that skin cancer primary prevention programmes should be maintained over several school years, rather than being employed a single time, to produce changes in the sun safety behaviour. In particular, because childhood is when individuals are more likely to adopt new attitudes and behaviour, parents should be targeted to teach sun protection skills to their children and promote skin cancer prevention behaviour in general.[9]

In terms of positively influencing sun protection in adolescents, appearance-based interventions may be effective in reducing skin cancer risk through reduced sun exposure.[8] This suggestion is based

	Total	Gender		
		Males	Females	
Hat wearing	24%	27%	20%	p<0.001
Sunscreen	44%	36%	51%	p<0.001
Sunglasses	36%	23%	49%	p<0.001
Protective clothing	20%	26%	14%	p<0.001
Brief clothing	22%	16%	28%	p<0.001
Stayed mainly in shade	29%	27%	31%	p<0.070
Stayed mainly inside	29%	32%	25%	p<0.001

Table 1. Percentage of Australian adolescents who reported that they usually or always engage in sun protection behaviours.[8]

on the observation that regular adoption of sun protection behaviours is low among Australian adolescents, ranging from 20% wearing protective clothing to 44 % using sunscreen (**Table 1**), with skin tone dissatisfaction, i.e. appearance concerns, playing a major role in this behaviour.[8] The issue of appearance-based reasons for poor sun safety behaviour by adolescents is reinforced by a US study of sunscreen and indoor tanning device use by high school students. It found a decline in sunscreen use by adolescents over a 10-year period, as well as high use of indoor tanning devices among females.[10] An additional consideration is that regular tanning may not necessarily be about looking good; rather, it may be about feeling good. A US researcher recently warned that tanning can be addictive (due to 'feel-good' endorphins flooding the body and brain as a result of UV hitting human skin).[11]

Fortunately, Australia does not have a sizeable indoor tanning industry largely due to campaigns against the practice and legislative controls.[5] Indeed, from 1st January 2015 an outright ban on commercial sunbeds will be in place in all Australian states, except Western Australia. In 2014, Auckland became the first city in New Zealand to ban sunbed use by those aged <18 years. Nonetheless, it would appear that skin cancer prevention efforts aimed at adolescents do need to take into account the relationship between skin tone dissatisfaction and their sun exposure behaviours.

Encouraging recent findings from Cancer Council Victoria's National Sun Protection Survey indicate that Australian adolescents may in fact be developing better attitudes towards tanning.[12] The survey revealed that 38% of Australian adolescents (aged 12-17 years) liked to get a sun tan during the summer of 2013-14 compared with 60% ten years earlier. There is also evidence that adolescents will spontaneously use shade if it is provided.[13,14] However, the National Sun Protection did show that adolescents were still not doing enough to protect themselves from the sun, with 23% still getting sunburnt during summer weekends, a figure that has not changed significantly since 2003-04.[12]

Given the risks associated with sunlight exposure during early life, regular sunscreen use as an adjunct to other forms of sun protection, especially protective clothing and hats, during childhood and adolescence, may be particularly important in reducing the lifetime incidence of skin cancer.[15,16]

Photoprotection and Sunscreen

Incident UV consists of UVA (320-400nm) and UVB (290-320nm), with UVA penetrating deeper into the skin to reach the dermis.[6] The energy of the UV as it passes through the skin is absorbed by DNA, lipids, and proteins, which results in direct and indirect damage to cellular structures. High-energy UVB rays cause direct damage to DNA (formation of thymine dimers) that has mutagenic potential and requires protection by DNA repair mechanisms. Indirect damage caused by both UVA and UVB radiation leads to the formation of reactive oxygen species (oxidative DNA damage), and activation of inflammatory cytokines. Collectively, these molecular insults result in sunburn, hyperpigmentation, premature aging, and photocarcinogenesis.[6]

The temporary protection against UV provided by sunscreens is due to their active ingredients, which are classified into organic or inorganic UV filters. Organic filters, such as the cinnamates and salicylates, are aromatic compounds that absorb UV. Inorganic filters are minerals, zinc oxide and titanium dioxide, that absorb, reflect, and scatter UV (**Figure 1**).[6]

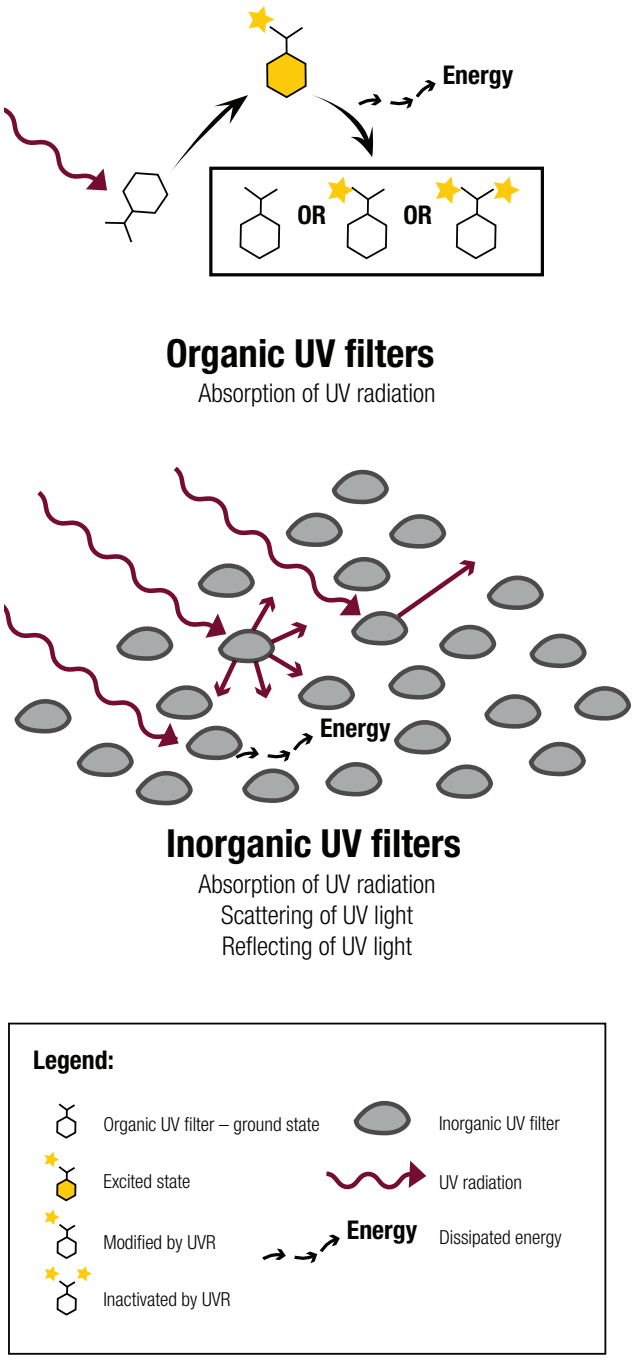

Figure 1. Mechanism of action of sunscreens. Organic UV filters absorb energy from UV causing electrons in the filter to jump to an excited state. On return to ground state, energy is released in the form of heat or light and the filter is potentially degraded. Inorganic UV filters can absorb, reflect, and scatter UV light and are more resistant to degradation than organic filters.[6]

In vitro skin models have demonstrated that application of sunscreen prior to UV exposure protects DNA from UV, which would be expected to reduce the risk of malignant transformation and photo-ageing.[17] The results of a recent *in vivo* study also indicate that sunscreens protect against cellular skin damage caused by UV exposure.[18] In the study, a high-sunscreen protection factor (SPF) sunscreen provided substantial protection against multiple cellular damage markers, including sunburn cells, Langerhans cells, thymine dimers, protein 53, and matrix metalloproteinase endpoints.[18]

A recent *in vivo* study demonstrated that sunscreen-protected mice took significantly longer to develop melanoma than unprotected mice when exposed to UV and developed significantly fewer melanomas.[19] However, it also found that sunscreen did not provide complete protection and UV exposure could still lead to melanoma, albeit at a reduced rate.[19] The mechanism for this appears to be UV-induced damage to the tumour-suppressing gene p53, which helps to protect the body from the effects of DNA damage.[19] The results of this study re-affirm that sunscreen is an important tool in the prevention of melanoma but also that, because sunscreen does not provide complete UV protection, it is equally important to also seek shade and wear appropriate clothing.

a)

b)

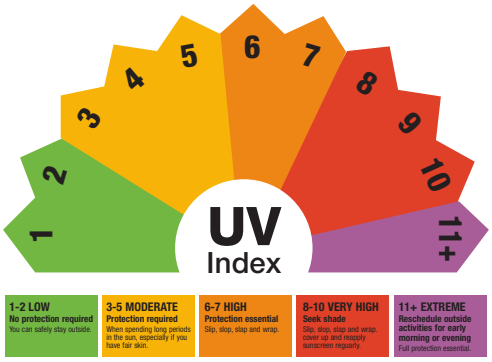

Figure 2. The Sun Protection Alert (**a**) has replaced the former UV Index (**b**) in New Zealand. It displays the beginning and end of the 'risk period' during a day and incorporates sun safety messages (e.g. seek shade, reapply sunscreen) that can be changed daily.[20]

In New Zealand, the Health Promotion Agency, MetService, and National Institute of Water and Atmospheric Research (NIWA), in consultation with the Cancer Society of New Zealand, have developed the new Sun Protection Alert (**Figure 2a**) to replace the UV Index (**Figure 2b**) as an improved tool for advising the general public the exact time when they should use sun protection anywhere in New Zealand.[20] The Sun Protection Alert was launched in November 2011 and is presented in weather forecasts via the Metservice website, newspapers, television and radio from the start of daylight savings until the end of April. Since 2013/14 it has also been part of the Metservice Smart Phone App.[20]

It is also worth noting that the regulatory guidelines for sunscreens were updated in 2013 with publication of the AS/NZS 2604/ISO 24443 standard.

Sunscreen Application and User Preference

Regular sunscreen use prevents the development of solar keratosis, squamous cell carcinoma, melanoma, and photo-ageing due to UV exposure.[6] However, these benefits are only realised if people apply sunscreen adequately, in addition to practicing other sun protection measures.[6] Unfortunately, sunscreen is often applied inadequately,[6,16,21-23] potentially leaving body areas without effective protection thus compromising the effectiveness of sunscreen as a sun protection modality.

The SPF afforded by a sunscreen is affected by application density.[15] Insufficient amounts, missing areas and exposure of the skin to UV exposure prior to sunscreen application are factors that undermine the protective efficacy of sunscreens in real life.[23] Instead of applying the internationally-agreed sunscreen thickness of 2 mg/cm^2 that is used to measure SPF, the actual amount of sunscreen used by most consumers is in the range 0.39-1.0 mg/cm^2, which results in a marked decrease in the effective SPF.[6,23]

Researchers emphasise that sunscreen application can be improved by consumer education.[21,23] For example, a newly developed systematised application technique (dose, apply, spread) that resulted in significantly more sunscreen being used (**Table 2**) as well as it being applied more evenly compared with a standard technique in a comparative study involving 58 child and adult volunteers could be included in an education campaign.[21] The systemised technique involved dividing the body and face into different segments so as not to forget any zone and comprised the following steps[21]

1. **Dose**: Visualisation of teaspoons to ensure the correct amount for each body segment;
2. **Apply**: Application of the total dose on several uniformly spaced spots for each body segment; and
3. **Spread**: Using circular movements, spread for an even application for each body segment).

A simple strategy of applying sunscreen before sun exposure and reapplying it once within one hour rather than encouraging the use of large amounts of sunscreen could also be promoted.[23] The early reapplication or use of very high-SPF sunscreen (SPF 70-100) is another possible strategy, the effectiveness of which was demonstrated by researchers who also revealed that sunscreen is typically applied insufficiently under 'real world' conditions.[22] It is worthwhile noting, however, that consumers choosing a sunscreen product that they like is important in encouraging its use.

	Usual technique (mean ± SD)	New technique (mean ± SD)	
Male volunteers	11.9±5.4g	18.0±7.8g	p=0.004
	0.6 mg/cm^2	1.0 mg/cm^2	p=0.004
Female volunteers	10.7±3.6g	17.2±6.0 g	p=0.001
	0.6 mg/cm^2	1.0 mg/cm^2	p=0.001
Children volunteers	8.8±4.1g	13.1±5.3g	p=0.004
	0.9 mg/cm^2	1.4 mg/cm^2	p=0.004

Table 2. Mean total quantity of sunscreen applied (g and mg/cm^2) using a new systematised application techinique (dose, apply, spread).[21]

Consumer guidance on sunscreen use, including how and when to apply, is provided on Australia's Therapeutic Goods Administration website: Sunscreens: Information for Consumers.

Adequate sun protection, including sunscreen use, is often neglected by outdoor workers,[24,25] who are at increased risk of skin cancer.[25-27] It has been proposed that sunscreens for those working outdoors should contain very high SPF, broad-spectrum, photo-stable filters for both UVB and UVA, and that they must be easy to apply and sweat resistant, and should not irritate the eyes.[24] In a randomised controlled study, >80% of the outdoor workers were fully satisfied with the cosmetic properties, sweat resistance, performance and usability of milk and gel sunscreen formulations used under outdoor working conditions.[24] The milk formulation was, however, rated as being slightly better than gel in terms of overall performance and significantly better with respect to ease of application.[24]

In terms of influencing the sun protection behaviour of outdoor workers, a systematic review undertaken by Australian researchers identified educational and multi-component interventions as being more successful in increasing sun protection in outdoor workers than policy or specific intervention components.[25] A highly relevant finding was the importance of including workers in the formulation of policies aimed at improving attitudes towards sun protection.[25]

UV Protection: Key Recommendations for Patients

1. Seek shade and minimise sun exposure, especially when the UV level is ≥3.
2. Wear protective clothing, i.e. a wide-brimmed hat, long-sleeve shirt, pants, and sunglasses
3. Use a broad-spectrum SPF30-50+ sunscreen every day.
4. For extended outdoor activity, use a water-resistant, broad-spectrum SPF≥50+ sunscreen.
5. Apply sunscreen liberally 15-20 minutes before going outdoors.
6. When outdoors, re-apply sunscreen at least every 2 hours, or immediately after swimming or excessive sweating.
7. Sunscreen should not be used to increase the amount of time spent outdoors.
8. Solariums or sunbeds should be avoided.

Sunscreen Adherence

Adherence to regular sunscreen use is a major challenge that potentially compromises the effectiveness of sunscreen as a sun protection modality.[6]

A group of French investigators has assessed factors underlying lack of patient adherence to sun protective measures.[28] Analysis of responses to a self-administered questionnaire distributed to dermatology patients receiving a sunscreen prescription, revealed a complex relationship between UV exposure, knowledge about UV-associated risks, and knowledge about sun protection recommendations and behaviour. The investigators recommended that future skin cancer prevention programmes should focus on specific populations with low sun protection behaviour and high UV exposure.[28]

It was subsequently observed that the French study overlooked a potentially important aspect of adherence, that of patient preference.[29] An important component of good clinical practice is shared decision-making and consideration of patient choice, perhaps best exemplified by dermatology and the use of emollients.[29] In this setting, patient adherence with therapy is facilitated when they are encouraged to choose an emollient of their choice, with the preference often being for lighter cream-based emollients to greasier ointments.[29]

There is also evidence that sun exposure habits and the propensity to undertake sun protection differ between individuals.[30] Swedish researchers investigated, in a primary healthcare population, the relationship between sun exposure habits/sun protection behaviour (including sunscreen use) and gender, age, educational level, and skin UV-sensitivity.[30] They found that, in addition to age, gender, educational level and skin type were also important factors affecting sun exposure habits and sun protection behaviour, thus supporting the strategy of individualising sun protection advice according to an individual patient's situation and capabilities.[30]

Sunscreen Controversies

Despite the well-established benefits of UV protection, controversies have arisen regarding the safety and efficacy of sunscreens. These include sunscreen being a cause of vitamin D deficiency and sunscreen ingredients, such as oxybenzone and nanoparticles of zinc oxide and titanium, being toxic.[5,15,16,31] However, reviews of the published literature indicate that the topical use of sunscreen protects against skin cancer but does not cause sub-normal vitamin D levels and has not been associated with systemic toxicity in humans.[15,16,31] For example, a randomised double-blind study by Marks and colleagues demonstrated that daily use of a broad-spectrum SPF17 sunscreen over the summer season was not associated with sub-normal vitamin D levels in Australian adults.[32] Regarding consumer concerns that nanoparticles in sunscreen might be absorbed into the bloodstream, the Australian Therapeutic Goods Administration states that nanoparticles are not a risk to health.

Further addressing concerns about vitamin D deficiency, at least one commentator has cautioned that strict sun avoidance should not be advocated given that vitamin D deficiency has become a health issue in Caucasian populations, not least because the effects of stringent sun avoidance on vitamin D levels may take years to manifest.[33] In this respect, it is reassuring that New Zealand researchers have demonstrated that exposure of the hands, face, and neck (10% of skin surface area) for about 3 minutes per day in the Auckland summer (through to about 60 minutes per day in the Invercargill winter) is sufficient to maintain normal vitamin D levels.[34] The researchers noted that the exposure durations demonstrated are well below those that produce erythema.[34] Furthermore, the results of the Marks et al study suggest that sufficient sunlight is received over an Australian summer, probably via both the sunscreen itself and the lack of total skin cover at all times, to allow adequate vitamin D synthesis in people who use sunscreen regularly.[32]

Another commentator has suggested that increased media coverage of the possible health benefits of vitamin D has not benefited skin cancer prevention campaign efforts.[5] In Australia, there is evidence that some people may be more likely to deliberately increase the time they spend out in the sun to increase their vitamin D levels.[5] Hence, intensified effort is required to raise awareness of the risks associated with UV exposure and times of the day and year when sun protection is required and what activities cause sunburn.[5] Individuals could also be dissuaded from attaining vitamin D through excessive UV exposure; for example, dietary supplementation of vitamin D provides an alternative reliable means of attaining adequate serum levels.[6]

A prevalent perception is that sunburn occurs mainly during water-based activities, such as at the beach.[5] However, there is data showing that most people actually get sunburnt during home-based activities such as gardening or other activity around the home.[5] Certainly, a need for improved sun-protective behaviours among young Australian adult sport competitors has been demonstrated.[35] Accordingly it has been proposed that skin cancer prevention campaigns should highlight that sun protection should include all outdoor activities and that health promotion efforts to increase levels of physical activity are best combined with sun protection messages.[5,35]

EXPERT'S CONCLUDING COMMENTS – *Louise Reiche*

Culturally, Australians and New Zealanders love the outdoors and being active outdoors is beneficial for cardiovascular, musculoskeletal, psychological and overall wellbeing. Excessive intermittent and cumulative UV exposure, however, generates skin cancers and photo-ageing and thus is costly (in human and financial terms) due to increased morbidity and sometimes death. So, encouraging activity whilst routinely adopting holistic sun protection strategies throughout life supports optimal health. In those already sun-damaged, gradual and progressive repair is seen in clinical practice – the more rigorously and longer patients practice sun protection the more likely there will be a resultant reduction of actinic keratoses, slowing skin cancer development, and photo-rejuvenation. Hence, it is never too late to begin looking after one's skin.

New Zealanders enjoy the sun for warmth much of the year and are better at reaching for sunscreen on bright sunny and hot days. They are often caught out and get sunburnt on cooler, windy or cloudy days. Planning activities attentive to the time of the day, under building, temporary or natural shade, while wearing hats, high ultra-protection factor (UPF) clothing suited to relevant activity and wrap around UV-protective sunglasses combined with sunscreen need to become habitual and integrated into Australasian culture across all ages. Obtaining more input from various sectors (particularly adolescents, sports people and outdoor workers) regarding practicalities and desirability of each of these measures should forge better future adherence.

Pharmaceutical-manufacturing progress in producing better tolerated (e.g. hypoallergenic, moisturising cream base for dry skin, non-oily milks, lotions, gels, and sprays for oily or hairy skin), user friendly and efficacious sunscreens (e.g. upgrading recommended SPF standards in response to what is required for sun protection on real human skin compared to 2 mg/cm^2 laboratory assessments) is immensely helpful in this regard. Applying a sunscreen that is inexpensive, never stains clothing and is required only once daily, is what consumers would prefer and is the next challenge for manufacturers.

EXPERT'S CONCLUDING COMMENTS – *Craig Sinclair*

Skin cancer represents the most costly cancer burden on our public health system and causes significant mortality and morbidity. This is largely because we are predominately a fair-skinned population living in a very high UV environment where sunburn can occur on fair skin within a very short period of exposure.

Given the intensity of our UV environment, it is critically important that we continue to promote the importance of sun protection to the general population and patients. Most people get sunburnt doing activity in around their home and at temperatures when it is comfortable to spend long periods outdoors.

There should be no concern that vitamin D levels are lower than what they should be due to the efforts of sun protection campaigns. Only a few minutes of UV exposure on most days of the week is all that is required to maintain adequate vitamin D levels at the time of the year when sun protection is required (UV Index >3). Vitamin D insufficiency in the general population is largely confined to winter months when sun protection for most Australian states is not a relevant public health message.

In Australia and New Zealand, sunscreens are developed to a high standard and are a very good adjunct to other forms of sun protection such as hats, shade and protective clothing.

Given the significant financial and human cost of skin cancer, now is not the time to be slowing down efforts to encourage sun protection and we must continue to further restrict indoor tanning use. Importantly we need a long-term and sustainable commitment to skin cancer prevention to ensure reductions in skin cancer incidence and mortality can continue to be achieved well into the future.

Take-Home Messages

- The prevention of skin cancer, especially melanoma, should begin in childhood and continue throughout adult life via adopting sun protection behaviour.
- Promoting sun protection, especially among children and adolescents, needs to continue to be a priority.
- Physician awareness of controversies associated with sunscreen use, e.g. vitamin D deficiency and ingredient toxicity, is necessary to counsel patients who have sunscreen concerns.
- Physicians should be familiar with sunscreen formulation, proper use, and benefits while encouraging adherence.
- Inadequate application and adherence remain challenges that limit the effectiveness of sunscreen use.
- Sun protection measures should be individualised according to a user's specific situation, preferences, and capabilities.
- SPF50+ sunscreen use continues to be a means of UV protection for the general public, offering benefits that outweigh potential risks.
- SPF50+ sunscreen should be used in combination with other UV protection behaviours.

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