

*Point/Counterpoint***Point: Sunscreen Use Is a Safe and Effective Approach to Skin Cancer Prevention**Adèle C. Green<sup>1</sup> and Gail M. Williams<sup>2</sup><sup>1</sup>Population Studies and Human Genetics Division, Queensland Institute of Medical Research and<sup>2</sup>School of Population Health, University of Queensland, Brisbane, Australia

Sunscreens are an adjunct to clothing and other physical means of solar UV radiation protection. Earlier sunscreens filtered mostly the high-energy UVB wavelengths (290-320 nm), but more recent broad-spectrum products can effectively absorb the longer UVA wavelengths (320-400 nm) as well (1-3). Acute UVB exposure is responsible for erythema (redness of the skin) and sunburn, but both UVA and UVB are responsible for suppression of skin immunity and for skin carcinogenesis in the long term so that broad-spectrum sunscreen use is required for skin cancer prevention (2-4).

The sun protection factor is the measure of protection of a sunscreen (weighted for UVB wavelengths) when it is applied uniformly to the skin at a thickness of 2 mg/cm<sup>2</sup>. The sun protection factor is a ratio of the protected to unprotected minimal erythemal dose and is nonlinear, such that sun protection factors SPF-15 and SPF-45 sunscreens filter 93% and 98% of UVB radiation, respectively (5). In a recent review of the safety of current UV filters and sunscreen products, Nash (6) pointed out that nearly all UV filters in currently marketed sunscreens have been evaluated for safety and efficacy in some capacity. Indeed most concerns about safety, such as photoactivation of sunscreen components, endocrine disruption, vitamin D deficiency, or increased risk of melanoma among sunscreen users remain unsupported by human evidence and more often relate to the way sunscreens are used than to concerns about their chemical components or spectral coverage (2, 6-9). For instance, sunscreens can be used by sunbathers as a means to intentionally increase their sun exposure (10), thus removing the context for standard safety assurance (as with the "misuse" of any product).

To properly evaluate long-term sunscreen effectiveness in humans, evidence from randomized controlled trials is required, principally because observational studies of sunscreen use and skin cancer suffer from intractable confounding: the determinants of sunscreen use and of skin cancer, e.g., susceptibility to sunburn, high sun exposure (occupational/recreational), past history of skin

cancer, are inseparable. Case control studies also lack the ability to relate timing of past sunscreen use to the development of skin cancers, whether melanoma, basal cell carcinoma (BCC), or squamous cell carcinomas. Moreover, sunscreens used by adults in 20th century observational studies have been superseded many times over so results of such studies will be largely irrelevant to 21st century skin cancer experiences (11). Likely, heterogeneity in the causal pathways of melanoma (12) and BCC (13) and the importance of childhood versus adult sun exposure in their development (14, 15) may further obscure observed relationships between these skin cancers and sunscreen use.

Thus, the strongest available evidence that sunscreen use is a safe and effective approach to prevention of skin cancer comes from the results of a 4.5-year community-based randomized controlled trial among 1,621 adult residents of Nambour, a subtropical Australian township. In comparison with people randomized to using sunscreen at their discretion if at all, people randomized to daily use of a broad-spectrum SPF15+ sunscreen showed a 40% reduction in squamous cell carcinoma tumors at the conclusion of the trial (16). During the trial, 75% of participants assigned to daily sunscreen use applied sunscreen to their head, neck, arms, and hands at least 3 or 4 d/wk, and a similar percentage of those not assigned to the sunscreen group either did not apply sunscreen or applied it no more than 1 or 2 d/wk. Although there was no effect on BCC incidence during the trial period, there was a trend of increasing intervals between BCCs among daily compared with discretionary sunscreen users who developed multiple BCCs (17). Eight years after cessation of the 4.5-year sunscreen intervention, participants who had been randomized to daily sunscreen use continued to show a 40% decrease in squamous cell carcinoma incidence (18). Their BCC incidence was also 25% lower in the last 4 years of posttrial follow-up, although not significantly so. Although most of the prolonged effectiveness could be attributed to the allocated daily sunscreen application during the trial, the prolongation of effect was enhanced by a more frequent use of sunscreen persisting in the intervention group more than in the control group in the follow-up period (25% versus 18%; ref. 19).

Currently, there is no such evidence to answer the question of the relationship between sunscreen use and the incidence of cutaneous melanoma. Trial data have shown however that incidence of benign melanocytic nevi, the strongest markers of melanoma risk, is reduced

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in children by sunscreen use (20). Furthermore in several short-term trials (21-23), regular sunscreen use has been shown to reduce the occurrence of solar keratoses, the benign squamous cell tumors that strongly determine not only risk of squamous cell carcinoma but also of BCC (24) and melanoma (12).

Adverse effects observed in the above trials included development of allergic contact dermatitis, photoallergic and phototoxic effects, stinging of the eyes, and interference with perspiration (16, 25). Again, there is no convincing evidence that long-term use of sunscreen causes either unsafe reduction in vitamin D levels or increased risk of melanoma (11, 26-29).

In conclusion, broad-spectrum sunscreens are an important part of skin cancer prevention, but not the whole solution. When used as an adjunct to protect skin from harmful UV exposure, broad-spectrum sunscreen can prevent occurrence of squamous cell skin cancers safely and effectively. Existing data from randomized controlled trials evaluating sunscreen use that show reduction in solar keratoses (markers of increased risk of melanoma and BCC), a suggestion of long-term BCC reduction in adults and in children, decreases in melanocytic nevi (melanoma risk-markers/precursors) are not inconsistent with the ultimate preventability of BCC and melanoma by sunscreen as well. Currently, however, evidence of effective prevention of BCC and melanoma by broad-spectrum sunscreen use remains insufficient.

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