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Associations between Silicone Skin Cast Score, Cumulative Sun Exposure, and Other Factors in the Ausimmune Study: A Multicenter Australian Study

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Abstract

Past sun exposure is linked to a wide range of disease outcomes but is difficult to measure accurately. Silicone skin casts measure skin damage, but some studies show that age rather than sun exposure is the most important determinant of cast score. We examined skin damage scores from silicone casts of the back of the hand in a large adult sample (n = 534) with a broad range of past cumulative UV radiation (UVR) doses. Participants were ages 18 to 61 years and resided in one of four locations down the eastern Australian seaboard, spanning 27-43°S. Data were collected by questionnaire and during a nurse-led interview and examination. Silicone casts were graded from 1 to 6, where higher score represents greater damage. Higher skin damage score was associated with lighter skin pigmentation [adjusted odds ratio (AOR), 4.51; 95% confidence interval (95% CI), 2.33-8.75], fairer natural hair color, particularly red hair (AOR, 11.31; 95% CI, 4.08-31.36), and blue/gray eyes (AOR, 1.72; 95% CI, 1.14-2.59). Higher cumulative UVR dose, particularly before age 18 years, was associated with higher skin damage score (AOR, 2.06; 95% CI, 1.15-2.67 per 1,000 KJ/m^2), as was number of sunburns, even after adjustment for cumulative UVR dose (AOR, 2.86; 95% CI, 1.50-5.43 for >10 sunburns ever compared with no sunburns ever). Silicone casts of the dorsum of the hand provide a measure of cumulative UVR dose and number of sunburns over the lifetime, which persists after adjustment for chronological age. They can be used as an objective measure of cumulative past sun exposure in epidemiologic studies, but other determinants of skin damage, such as skin pigmentation, should be concurrently evaluated. (Cancer Epidemiol Biomarkers Prev 2009;18(11):2887–94)

Introduction

Over the past 40 years, an increasing number of diseases have been linked to sun exposure (1). Initially, research was predominantly stimulated by concern about the effects of excess sun exposure and highlighted adverse health outcomes related to the skin and eyes: skin cancers, cataracts, and pterygia (2). More recently, there has been considerable interest in possible beneficial effects of sun exposure through vitamin D–mediated effects on immunomodulation and cancer risk reduction (3-7).

A recurrent issue has been the difficulty of measuring personal past sun exposure over the life course. In response to this need, several innovative methods have arisen. For example, recall of past sun exposure has been aided by the use of a personal work and residence calendar (8, 9), linking recalled sun exposure to other memorable events across the life course, such as location of residence. Objective measures of recent and chronic sun exposure have also been developed. For the former, spectrophotometric measurements of sun-exposed and nonexposed skin provide both a measure of the natural skin color and the change from that due to recent sun exposure (10). For chronic sun exposure, silicone rubber imprints of the skin, usually on the back of the hand, have been used to record changes in skin texture thought to be a sign of photoaging (9). Histologically, the latter includes loss and disorganization of collagen fibrils, thickening of the stratum corneum, stratum granulosum, and epidermis, and abnormal accumulation of elastin (11, 12). In 1980, Beagley and Gibson developed a scoring system to quantify the degree of photoaging based on the pattern of lines on these skin casts (12). However, most previous studies have not been large enough to unravel the separate effects of chronological aging and cumulative sun damage on the development of photoaging. Furthermore, although several researchers have examined previously the determinants of change in cast score (12-16), this has been confined to particular age or racial groups or single locations, possibly limiting the variation in the causative exposures.

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Here, we aim to identify the determinants of skin damage, as measured by silicone rubber skin casts of the back of the hand, in relation to a wide range of environmental factors, in young and middle-aged adults living in four regions of Australia: from a high ambient UV radiation (UVR) region, Queensland, to the lower ambient UVR region of Tasmania. In particular, we aim to assess the effect of cumulative sun exposure (derived from both time in sun and ambient UVR at residence over the life course) after taking into account chronological age and skin phenotype.

Materials and Methods

Current analyses are based on the control group ($n = 534$) of the Ausimmune Study. This is a multicenter case-control study examining environmental risk factors for a first clinical diagnosis of central nervous system demyelination in four study centers across a latitudinal gradient from 27°S to 43°S down the eastern seaboard of Australia. The details of control recruitment in the Ausimmune Study are described elsewhere (17). Essentially, controls were randomly selected from the Australian Electoral Roll in each of the study regions and matched on age (within 2 years) and sex to a participating case (ages 18-59 years and has had a first clinical diagnosis). Controls were thus ages 18 to 61 years (because 18 years is the minimum age for the Australian Electoral Roll) but with the strong female preponderance expected for the first clinical diagnosis cases.

Participants completed a self-administered questionnaire, including questions on ancestry (self-identified and country of birth of parents and grandparents); use of vitamin or mineral supplements; occupation (including whether mainly indoor or outdoor); education (highest education completed, in three categories); and smoking history as well as a personal work and residence calendar noting location of residence, hours per day outdoors in summer and winter, and occupation (where applicable) for every year of life. During a face-to-face interview with a study nurse, participants provided data on typical sun exposure and the use of sunscreen and sun protective clothing during different age periods.

The study nurses were trained to carry out skin assessments and the study coordinator conducted regular site visits to ensure standardization of data collection across study regions. Study nurses assessed natural skin type, and eye and hair color, in consultation with study participants and with reference to color photographs, to ensure standardization in coding. Nurses also undertook nevi counts of the left arm (18) using the IARC protocol (19) and examined for the presence of pterygia and solar keratoses (the latter on the face or hands). In addition, skin pigmentation was assessed by measuring skin reflectance at exposed (hand and shoulder) and nonexposed (upper inner arm and buttock) skin sites using a spectrophotometer (Minolta CM2500d) with measurements at 400 and 420 nm wavelengths (20). Silicone rubber casts of the back of the hand were taken as follows: a small amount of silicone liquid was mixed with catalyst and applied to the dorsum of the hand, avoiding major veins, visible skin blemishes, scars, etc. After 7 min, the cast was removed, allowed to dry, and stored in a labeled bag until grading (12).

Silicone casts were graded by an independent grader who was blind to any other data on the participants. Left-hand casts were graded, except where these were unavailable (e.g., left-hand unsuitable for making a cast) or the cast was of insufficient quality to be gradable. Casts were photographed and graded using the digital images. Casts were graded in batches, with some casts blindly reinserted in a subsequent batch (with the grader blinded to the inclusion of the repeat casts) to determine intrarater grading reliability across batches.

Statistical Analysis. The goal of this analysis was to verify that the skin cast grades (skin damage scores) provided a measure of cumulative UVR dose (a function of both ambient UVR and time in the sun) across the life course, taking account of skin sun sensitivity and natural pigmentation. Skin casts were scored on a scale from 1 to 6 (minimal to maximal damage) and treated as an ordinal categorical variable.

We converted spectrophotometer readings to measures of melanin density according to previously validated work (21). As previous work has shown that upper inner arm melanin density (one measure of natural skin pigmentation) varies seasonally (21), we used buttock melanin density as the measure of unexposed skin color.

From the latitude and longitude of the location of residence, and using satellite-derived estimates of ground-level ambient UVR, we estimated the average daily ambient erythemal UVR (J/m^2) for each month of each year of life. The UVR data are derived from a predictive model (22) using satellite measurements from the Total Ozone Mapping Spectrometer.[9] We calculated the average daily ambient erythemal UVR for each 5-year period and for the summer and winter months of each year of life, averaged over 5 years. We used these data and the self-reported hours outside in the sun during summer and winter weekends and holidays (for each year of life) to calculate the personal cumulative leisure-time UVR dose for each participant (KJ/m^2). We used leisure-time UVR dose, as this measure has been found previously to have a higher correlation with actinic damage than total sun exposure (including both leisure and occupational exposure) in an Australian setting (23).

We used Cohen's κ to assess intrarater reliability for casts with repeat scores and proportional odds ordinal logistic regression to examine the determinants of skin damage as rated by the skin damage score. In the ordinal logistic regression model, the interpretation of an odds ratio (OR) is that, for each of the five possible splits in the scores, such as <3 versus ≥ 3, the OR expresses the effect of the covariate on the odds of being above the split rather than below. It is an assumption of the model (the proportional odds assumption) that these five ratios (for six categories as here) are all the same for a given covariate. We assessed the validity of this assumption using Brant's method (24). All analyses were undertaken in Stata 9.2 (StataCorp).

This study was approved by the Human Research Ethics Committee of the Australian National University. All participants signed informed consent before participation.

[9] Accessed from http://iridl.ldeo.columbia.edu/SOURCES/NASA/GSFC/TOMS/.

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Results

General Features. Study participants were ages between 18 and 61 years, with a female preponderance (see Table 1), reflecting the gender distribution of the case population. Of 1,118 controls initially selected, 937 (84%) were successfully contacted, and a "conclusive outcome" (eligible versus not eligible) could not be reached for 181 (e.g., there was no listed telephone number and the possible participant was no longer resident at the available address). Of the 548 who participated in the study (58% of those contacted), 534 provided a gradable silicone cast. Skin damage scores ranged from 2 to 6, with a higher score reflecting higher skin damage. In the relatively high ambient UVR environment of Australia, there were no skin damage scores of 1. Females were less likely to have actinic damage than males and there was a strong, linear, dose response of increasing skin damage score with increasing age (Table 1). Age was used as a continuous covariate in all subsequent regression analyses. Variation in skin damage score by age was particularly marked in the Brisbane study sample, where there was a clear progression to higher score with increasing age (see Fig. 1). After accounting for these gender and age effects, Table 1 shows that Caucasians were four times more likely to have actinic damage than non-Caucasians, and Australian-born subjects were more likely to have cast damage. Among immigrants, age at migration was inversely related to cast damage (Table 1) and this effect persisted after further adjustment for skin pigmentation [age of arrival in Australia, 0-9 years: adjusted OR (AOR), 0.64; 95% confidence interval (95% CI), 0.28-1.44; 10-19 years: AOR, 0.41; 95% CI, 0.17-0.99; ≥20 years: AOR, 0.34; 95% CI, 0.15-0.77 compared with the reference category of "Australian-born"]. Thus, the effect is not due to lower skin damage in deeper pigmented late arrivals to Australia but more likely reflects longer exposure to the high ambient UVR Australian environment. Most of the study sample was of British/Irish descent (having at least two such grandparents, $n = 288$); for 225 participants, all four grandparents were British/Irish. Compared with the latter group, those with at least one European grandparent (AOR, 0.75 (95% CI 0.52-1.08) or one Asian grandparent (AOR, 0.26; 95% CI, 0.13-0.55) had lower odds of having a higher cast score. Although there was no evidence of latitudinal variation in the skin damage score overall, in the subgroup who had always lived within the current state of residence, there was a borderline statistically significant trend of decreasing skin damage score with increasing latitude ($P = 0.05$).

We examined how study process factors related to cast damage score. There was no association between the skin damage score and the season of the year in which the cast was made ($P = 0.76$). Right-hand casts had significantly higher cast scores than left-hand casts (OR, 3.45; 95% CI, 1.61-7.43); thus, further analyses were also adjusted for this factor. Previous work has shown similar asymmetric sun damage due to the asymmetric nature of sun exposure during automobile driving (25): driving on the left-hand side of the road in Australia means that the right side of the face and the right hand receive more sun exposure than the left. There was good agreement on blinded repeat scoring of a random selection of skin casts ($n = 51$), with Cohen's $\kappa = 0.95$ (95% CI, 0.85-1.00).

Table 1. Skin damage score in relation to demographic characteristics of study group

	n (%)	Cast score, mean (SD)	Unadjusted OR (95% CI)	AOR* (95% CI)
Age (y)				
18-29	92 (17.2)	3.0 (1.4)	1.00 (reference)	1.00 (reference)
30-39	184 (34.5)	3.6 (1.2)	2.83 (1.76-4.55)	2.76 (1.71-4.46)
40-49	166 (31.1)	4.6 (1.1)	10.80 (6.52-17.90)	10.70 (6.44-17.80)
50-59	92 (17.2)	4.9 (1.1)	19.96 (11.24-35.44)	21.14 (11.83-37.79)
Total	534		$P < 0.001$	$P < 0.001$
Sex				
Male	114 (21.4)	4.2 (1.3)	1.00 (reference)	1.00 (reference)
Female	420 (78.7)	4.0 (1.4)	0.71 (0.49-1.02)	0.54 (0.37-0.79)
			$P = 0.065$	$P = 0.002$
Location				
Brisbane (27°S)	178 (33.3)	4.0 (1.4)	1.00 (reference)	1.00 (reference)
Newcastle (33°S)	99 (18.5)	4.1 (1.5)	1.12 (0.71-1.75)	1.03 (0.65-1.63)
Geelong (37°S)	142 (26.6)	3.8 (1.2)	0.85 (0.58-1.26)	0.69 (0.46-1.03)
Tasmania (43°S)	115 (21.5)	4.3 (1.3)	1.58 (1.05-2.40)	1.07 (0.69-1.65)
			$P = 0.11$	$P = 0.74$
Caucasian				
No	27 (5.1)	3.37 (1.47)	1.00 (reference)	1.00 (reference)
Yes	506 (94.9)	4.07 (1.33)	2.87 (1.35-6.11)	4.36 (1.94-9.80)
Country of birth				
Australia	470	4.07 (1.34)	Reference	Reference
Other†	61	3.79 (1.32)	0.70 (0.44-1.13)	0.40 (0.24-0.65)
Age arrived in Australia				
Australian-born	470	4.07 (1.34)	1.00 (reference)	1.00 (reference)
0-9 y	20	3.95 (1.23)	0.90 (0.42-1.92)	0.77 (0.35-1.69)
10-19 y	16	3.63 (1.20)	0.58 (0.25-1.36)	0.34 (0.15-0.81)
>20 y	25	3.76 (1.48)	0.65 (0.31-1.37)	0.23 (0.10-0.50)
				$P_{trend} < 0.001$
Hand of cast				
Left	511	3.99 (1.34)	1.00 (reference)	1.00 (reference)
Right	23	4.91 (1.16)	3.45 (1.61-7.43)	3.45 (1.54-7.74)

*Adjusted for age, sex (where appropriate), and left/right cast; see text for model details.
†Other includes northern Europe, United Kingdom, South Africa, New Zealand, Southeast Asia, Africa, and the Pacific Islands.

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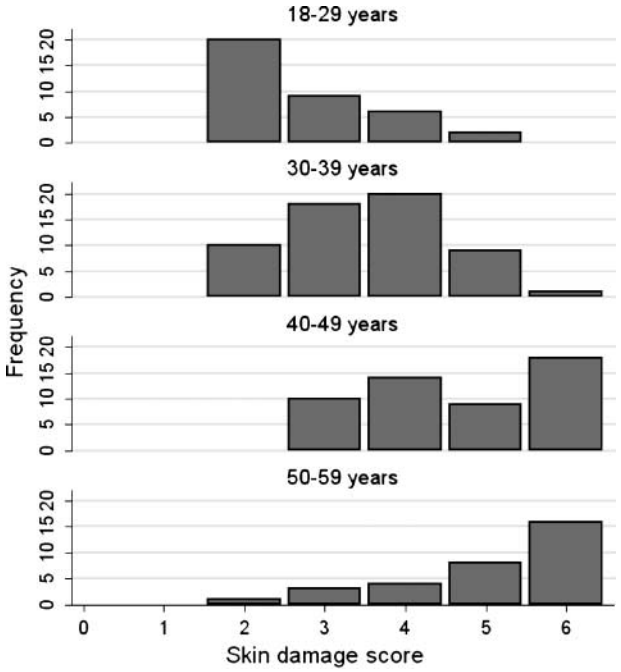

Figure 1. Skin damage score by age group in the Brisbane study region.

Pigmentary Traits and Sun Sensitivity. Fairer natural skin color, measured both objectively using skin spectrophotometry of body locations unlikely to receive sun exposure (buttock and upper inner arm) and subjectively by participant self-report in relation to photographic images, was associated ($P < 0.001$) with increased odds of having a high skin damage score (Table 2). For every 1% increase in buttock melanin density, the AOR for skin damage score was 0.72 (95% CI, 0.64-0.82). Hair color was also important: redheads were >10 times more likely to have a higher cast score compared with those with naturally black hair (Table 2). Similarly, lighter eye color showed increased odds of having a higher skin damage score. Of interest, the adverse effect of lighter skin pigmentation or fairer hair or eye color increased after adjustment for cumulative UVR dose, with AOR (95% CI) of 4.51 (2.33-8.75), 11.31 (4.08-31.36), and 1.72 (1.14-2.59), respectively. This reflects that these phenotypes were all less likely to be UVR exposed.

Participants in the highest category of self-reported teenage freckling had a 6-fold increased risk of higher skin damage score compared with those with no freckles. However, we found no association in the adjusted analyses between self-reported number of moles as a teenager and skin damage score. There was an almost 2-fold increased risk of having a high skin damage score with past history of any blistering sunburn, and a greater number of past sunburns was associated with increased odds of higher skin damage score. In crude analyses, sunscreen use, particularly before age 20 years, appeared to be associated with decreased odds of a higher skin damage score (OR, 0.30; 95% CI, 0.15-0.60) for always using sunscreen in summer compared with never using sunscreen at ages 11 to 15 years ($P_{trend} < 0.001$). This effect was, however, markedly attenuated after adjustment for age and sex (OR, 0.72; 95% CI, 0.36-1.43; $P_{trend} = 0.83$), with minimal further change in the fully adjusted model (AOR, 0.65; 95% CI, 0.32-1.29; $P_{trend} = 0.45$).

Past Sun Exposure. In this sample, there was a wide distribution of cumulative sun exposure as shown in Fig. 2. Even among subjects ages 18 to 25 years ($n = 35$), the cumulative leisure-time UVR dose was widely distributed (median, 1.9 KJ/m^2; interquartile range, 0.49 KJ/m^2).

Higher self-reported time in the sun was associated with higher skin damage score, particularly for sun exposure during the early years of life (up to age 18 years) for both summer and winter exposure (Table 3). Using the calendar data to calculate a "UVR dose" for leisure time (weekends and holidays) for every year of life and accumulating this over the life course, higher cumulative UVR dose was associated with higher skin damage score, with a larger magnitude of effect for early-life exposure (6-18 years; AOR, 2.06) than for lifetime UV exposure (AOR, 1.39). Interestingly, Table 2 shows that sunburn history predicts actinic damage independent of cumulative sun exposure. In fact, the two measures were poorly correlated (Spearman's $\sigma = 0.07$; $P = 0.11$).

Lifestyle Factors and Pregnancy. We found no association between skin damage score and current smoking, ever smoking, or total pack-years smoked. Similarly, higher levels of physical activity and body mass index were not associated with the skin damage score. There was no evidence that use of dietary supplements overall, or specifically antioxidants or omega-3 or omega-6, influenced the skin damage score. A university education (compared with 3 years of high school or less) was associated with decreased odds of higher skin damage (AOR, 0.68; 95% CI, 0.45-1.05), whereas, compared with managers, all other occupational groups tended to have higher skin damage scores, with the strongest effect for tradespersons (AOR, 2.47; 95% CI, 1.20-5.11). Overall, the indoor/outdoor classification of occupation was not associated with skin damage score, although there was a difference between sexes: whereas there was no association in women, outdoors occupation entailed an increased odds of having a higher cast score in men, which remained after adjustment for age, buttock melanin density, and whether it was a left or right cast. Thus, the risk gradient in men, relative to the "indoors" category, was "mainly indoors" (AOR, 2.13; 95% CI, 1.00-8.08), "half indoors" (AOR, 4.34; 95% CI, 1.66-11.37), and "mainly outdoors" (AOR, 4.62; 95% CI, 1.62-13.21).

Higher parity was associated with an increased skin damage score (OR, 1.52; 95% CI, 1.33-1.73) that persisted but was attenuated after adjustment for age, buttock melanin density, left or right cast and cumulative leisure-time UVR dose (AOR, 1.18; 95% CI, 1.02-1.36).

Other Indicators of Chronic Sun Exposure. Past history of solar keratosis was associated with a higher skin damage score and this association persisted after adjustment for age, sex, buttock melanin density, and cumulative UVR dose (Table 4). We found a strong inverse association between cast score and nevi count, particularly comparing those with any nevi with those with no nevi (AOR, 0.39; 95% CI, 0.23-0.66). For large nevi (>5 mm), the association reversed [compared with a reference of "no large nevi": 1-4 nevi (AOR, 1.04; 95% CI, 0.70-1.55) and ≥5 large nevi (AOR, 1.39; 95% CI, 0.65-2.95)]. A history of any skin cancer was associated with a higher skin damage score, but the estimate was relatively imprecise, reflecting

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a total of only 37 skin cancers in this relatively young age group. Although, in the univariate analyses, other indicators of higher past sun exposure, such as cataract and pterygium, were positively associated with higher skin damage score, these associations did not persist after adjustment for age, sex, and cumulative past UVR dose.

In these ordinal regression models, the assumption of proportional odds was satisfied in all but one case. Brant's method returned a statistically significant result ($P = 0.03$) for participant age, suggesting that the dependence of skin damage score on age was not parallel between all scores. However, to find a single moderately significant result among multiple tests is not surprising; overall, the assumption of proportional odds was well supported.

Discussion

In this multicenter study, several phenotypic and environmental factors were associated with increased skin damage

Table 2. Relationship of skin damage score to pigmentary traits and sun sensitivity

	n (%)	Unadjusted OR (95% CI)	AOR* (95% CI)
Natural skin color†			
Dark/olive	41 (8.0)	1.00 (reference)	1.00 (reference)
Olive/medium	110 (21.4)	2.34 (1.22-4.50)	3.62 (1.82-7.21)
Medium/fair	180 (35.0)	4.00 (2.14-7.50)	6.09 (3.14-11.80)
Fair	183 (35.6)	2.91 (1.56-5.44)	4.51 (2.33-8.75)
		$P_{trend} = 0.005$	$P_{trend} < 0.001$
Hair color†			
Black	29 (5.6)	1.00 (reference)	1.00 (reference)
Dark brown	195 (37.9)	1.77 (0.85-3.69)	2.88 (1.36-6.09)
Blonde	262 (51.0)	2.08 (1.01-4.29)	3.88 (1.85-8.16)
Red	28 (5.5)	5.05 (1.89-13.46)	11.31 (4.08-31.36)
		$P_{trend} = 0.003$	$P_{trend} < 0.001$
Eye color†			
Brown	115 (22.4)	1.00 (reference)	1.00 (reference)
Hazel	91 (17.7)	1.65 (1.01-2.69)	1.75 (1.06-2.91)
Green	66 (12.8)	1.10 (0.64-1.88)	1.42 (0.82-2.45)
Blue/gray	242 (47.1)	1.49 (1.01-2.20)	1.72 (1.14-2.59)
		$P_{trend} = 0.13$	$P_{trend} = 0.03$
Teen freckling‡			
No freckles	132 (25.6)	1.00 (reference)	1.00 (reference)
Few freckles	219 (42.5)	1.59 (1.08-2.34)	1.99 (1.33-2.98)
Some freckles	108 (21.0)	1.98 (1.26-3.12)	3.05 (1.89-4.94)
Many freckles	56 (10.9)	3.89 (2.20-6.90)	6.89 (3.70-12.83)
		$P_{trend} < 0.001$	$P_{trend} < 0.001$
Upper inner arm melanin density (per 1% increase)	*n* = 504 (range, -8.79 to 8.04)	0.89 (0.79-1.01)	0.81 (0.72-0.92)
		$P = 0.06$	$P = 0.001$
Buttock melanin density (per 1% increase)	*n* = 504 (range, -6.93 to 5.47)	0.78 (0.69-0.87)	0.72 (0.64-0.82)
		$P < 0.001$	$P < 0.001$
Reaction to first exposure to midday summer sun‡			
Never burn	20 (3.9)	1.00 (reference)	1.00 (reference)
Burn after >2 h	64 (12.4)	0.95 (0.39-2.31)	1.61 (0.61-4.26)
Burn after 1-2 h	137 (26.6)	1.17 (0.51-2.68)	2.61 (1.05-6.52)
Burn after 0.5-1 h	144 (28.0)	1.61 (0.70-3.68)	3.42 (1.37-8.54)
Burn after <0.5 h	150 (29.1)	1.35 (0.59-3.07)	3.15 (1.26-7.89)
		$P_{trend} = 0.11$	$P_{trend} = 0.003$
Reaction to 1 h of summer sun‡			
Burn then peel	203 (39.5)	1.00 (reference)	1.00 (reference)
Burn then tan	209 (40.7)	0.84 (0.60-1.19)	0.78 (0.54-1.11)
Tan only	102 (19.8)	0.65 (0.43-0.99)	0.43 (0.27-0.67)
		$P_{trend} = 0.05$	$P_{trend} < 0.001$
End of summer tan‡			
Dark	98 (19.1)	1.00 (reference)	1.00 (reference)
Medium	212 (41.3)	1.60 (1.03-2.47)	1.69 (1.07-2.66)
Light	136 (26.5)	1.52 (0.95-2.44)	1.91 (1.15-3.15)
No tan	68 (13.2)	1.65 (0.94-2.90)	2.65 (1.46-4.82)
		$P_{trend} = 0.13$	$P_{trend} = 0.002$
Past history of blistering sunburn‡			
No	172 (33.7)	1.00 (reference)	1.00 (reference)
Yes	338 (66.3)	2.17 (1.56-2.31)	1.97 (1.40-2.78)
		$P < 0.001$	$P < 0.001$
Number of sunburns in lifetime‡			
Never	69 (13.4)	1.00 (reference)	1.00 (reference)
Once	88 (17.1)	0.72 (0.41-1.26)	0.75 (0.42-1.35)
2-5 times	223 (43.3)	1.26 (0.78-2.02)	1.36 (0.82-2.25)
6-10 times	69 (13.4)	1.39 (0.77-2.51)	1.49 (0.80-2.77)
>10 times	66 (12.8)	2.53 (1.39-4.61)	2.86 (1.50-5.43)
		$P < 0.001$	$P < 0.001$

*Adjusted for left/right cast, age, sex, and cumulative UVR dose; see text for model details.
†By nurse observation.
‡By self-report.

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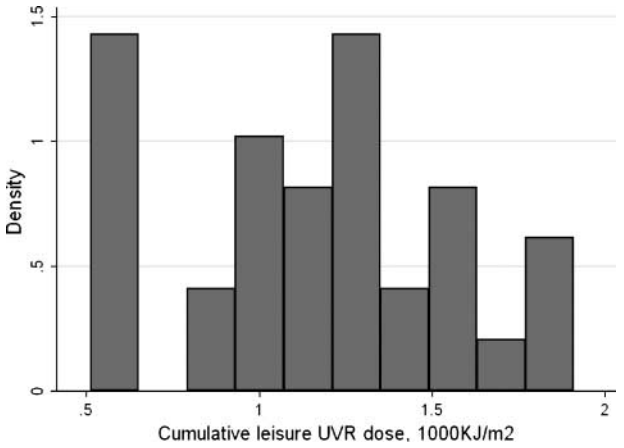

Figure 2. Variation in cumulative leisure-time UVR dose in participants ages 18 to 25 y.

as assessed by silicone cast score. In particular, the adverse effect of fair skin pigmentation increased after accounting for life-course sun exposure. It was shown that this reflects reduced sun exposure and probably increased sun protective behaviors in those with the fairest skin types. Sun exposure from ages 6 to 18 years was associated with a 2-fold increase in skin damage score, after accounting for current age at interview and other confounding factors. Individuals who were Australian-born (particularly compared with those born overseas and arriving in Australia after age 20 years) tended to have higher skin damage scores. This is consistent with the finding by English et al. of a decreasing risk of squamous cell carcinoma of the skin with later arrival in Australia compared with Australian-born (26). In contrast to other studies, we found no association with smoking (12), body mass index (16), or intake of antioxidants (assessed by dietary supplement history; ref. 27). Furthermore, latitude of residence was not strongly associated with skin damage score. This highlights that personal sun exposure behavior and host phenotype are also important to the development of skin damage, not just ambient UVR. Outdoor jobs were associated with increased skin damage but only in males. Fewer females reported mainly outdoor jobs (n = 15); further, women doing those jobs may be more likely to use sun protection than their male counterparts. Use of sunscreen at any life stage did not appear to affect skin damage score. However, sunscreen use has been widely promoted in Australia only since the 1980s. This means that, for many of our participants, sunscreen use would have been uncommon during their childhood years, a time that appears particularly important for the development of skin damage.

As with several other studies (12, 28), age was an important predictor of skin damage, here measured by silicone casts. Our findings are very similar to those of Battistuta et al. who found a 13% increase in the odds of higher cast score for every 1-year increase in age in a cohort of Queensland adults ages 18 to 79 years (12). Our corresponding finding was a 12% increase in odds for age in years as a continuous variable (OR, 1.12; 95% CI, 1.10-1.14). In addition to accounting for any direct effect of advancing years, age as a covariate might be expected to act as a surrogate for cumulative sun exposure; however, we found that, even after adjustment for age, cumulative sun exposure as measured by personal UVR dose remained associated with higher actinic damage. Although Seddon et al. suggested that skin microtopography measurement (using silicone casts) reflects intrinsic aging rather than sun-induced aging, our results do not support this (15). After adjustment for the equivalent factors to Seddon et al. (15), cumulative UVR exposure (from age 6 years to age of study participation) remained important, with elevated odds of skin damage (Table 3). These findings highlight the strength of this study with regard to large sample size (n = 534 compared with n = 115; ref. 15) and the study of healthy community controls compared with patients with melanoma in the Seddon et al. study (15). But perhaps most importantly, as our study regions ranged from high ambient UVR Brisbane (27°S) to low ambient UVR Tasmania (43°S), there was also a very wide range of personal UVR exposure within the study group, even within narrow age bands. Thus, we were able to disentangle the relative effects of cumulative sun exposure and chronological age. Other strengths included the precise measure of skin pigmentation by spectrophotometer and the ability to examine both constitutive phenotype (e.g., fair skin) and cumulative past sun exposure concurrently.

The finding of an inverse association between skin damage score and nevi count concurs with other work that

Table 3. Association between skin damage score and leisure-time sun exposure

	n	Unadjusted OR	OR (95% CI), adjusted for age and sex	Fully AOR* (95% CI)
Hours per day in sun in summer (ages 6-10 y)†	512	1.24 (1.09-1.42) P = 0.001	1.14 (1.00-1.33) P = 0.06	1.17 (1.01-1.35) P = 0.04
Hours per day in sun in winter (ages 6-10 y)†	512	1.20 (1.07-1.35) P = 0.002	1.14 (1.01-1.29) P = 0.03	1.17 (1.03-1.33) P = 0.01
Cumulative leisure-time sun exposure 6-18 y (per 1,000 KJ/m^2)‡	501	1.49 (0.88-2.52) P = 0.14	1.50 (0.86-2.63) P = 0.15	2.06 (1.15-2.67) P = 0.01
Cumulative leisure-time sun exposure 6 y-current age (per 1,000 KJ/m^2)	501	2.27 (1.90-2.70) P < 0.001	1.25 (1.00-1.56) P = 0.05	1.39 (1.11-1.75) P = 0.005

*Adjusted for age, sex, education, occupational group, buttock melanin density, and left/right cast; see text for model details.
†By self-report.
‡Cumulative UVR dose is total UV exposure from age 6 y to current (units are 1,000 KJ/m^2; range in these data, 0.51-5.87), that is, ambient UVR * self-reported time in sun.

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Table 4. Relationship between skin damage score and other signs of past sun exposure

	n	Unadjusted OR (95% CI)	OR (95% CI), adjusted for age and sex	Fully AOR* (95% CI)
Any pterygium†				
No	275	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	227	1.53 (1.12-2.09)	1.10 (0.80-1.52)	1.02 (0.73-1.42)
Any skin cancer‡				
No	463	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	37	2.64 (1.40-4.99)	1.71 (0.90-3.27)	1.74 (0.91-3.33)
Any solar keratosis‡				
No	375	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	122	3.14 (2.15-4.57)	1.67 (1.12-2.48)	1.55 (1.03-2.32)
Any cataract‡				
No	488	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	13	2.50 (0.98-6.36)	1.01 (0.37-2.78)	1.00 (0.36-2.80)
Any melanoma‡				
No	469	1.00 (reference)	1.00 (reference)	1.00 (reference)
Yes	31	2.96 (1.46-6.00)	2.01 (0.99-4.10)	1.92 (0.94-3.94)
Nevi count†				
0	57	1.00 (reference)	1.00 (reference)	1.00 (reference)
1-9	203	0.33 (0.20-0.57)	0.38 (0.22-0.67)	0.39 (0.22-0.68)
10-19	84	0.41 (0.22-0.75)	0.49 (0.26-0.91)	0.48 (0.25-0.90)
20-49	113	0.26 (0.15-0.47)	0.37 (0.20-0.67)	0.36 (0.20-0.67)
≥50	47	0.31 (0.15-0.63)	0.41 (0.20-0.84)	0.36 (0.17-0.75)
		P_{trend} = 0.002	P_{trend} = 0.07	P_{trend} = 0.04
Large nevi (>5 mm) count†				
0	394	1.00 (reference)	1.00 (reference)	1.00 (reference)
1-4	108	1.03 (0.71-1.50)	1.14 (0.77-1.67)	1.04 (0.70-1.55)
≥5	26	1.41 (0.68-2.90)	1.52 (0.73-3.17)	1.39 (0.65-2.95)
		P_{trend} = 0.45	P_{trend} = 0.24	P_{trend} = 0.48

*Adjusted for age, sex, buttock melanin density, left/right cast, and cumulative UVR dose; see text for model details.
†By nurse observation.
‡By self-report.

found the lowest nevi count in chronically sun-exposed skin (29, 30) or that with evidence of more skin damage (31). Higher nevi counts may be more related to intermittent high dose sun exposure (e.g., sunburns; ref. 29) or occur within a narrow UV dose range (30). Additionally, the inverse association may reflect UVR-induced nevus involution as suggested by Purdue et al. (32).

Our results should also be considered in the context of the limitations of the study. Firstly, control participants included here are not a random sample of the population but are matched to cases in a case-control study. Therefore, neither the age nor the sex distribution are those of the underlying population. However, controls were randomly selected from the Australian Electoral Roll for their region of residence and should be representative of the sex and 2-year age group from which they were selected. Secondly, the study relies on self-report data, including for sun exposure in the early years of life. As with previous studies examining early-life sun exposure, we have used a personal work and residence calendar to record data on each year of life, linking these data to events likely to be recalled with some accuracy (e.g., locations of residence) to aid recall. Finally, our data on amount of occupational sun exposure or sun exposure during the working week are limited: many participants did not record data during the school years or during breaks from the workforce, such as for parenting. However, we found that sun exposure during the early years of life was particularly associated with the skin cast score. In this age range, variability in sun exposure is probably most related to variability in leisure-time exposure, with variability in exposure during school hours more constrained. Furthermore, some researchers have noted that individuals may receive the greatest proportion of their cumulative sun exposure during the childhood and teenage years (33).

The silicone cast skin damage score was strongly associated with history of previous solar keratosis or skin cancer but not with pterygium or cataract. This may relate to different use of sun protection for the eyes compared with the skin and particularly for the back of the hand. Alternatively, presence or absence of pterygium may be difficult to ascertain (by nurse examination), and as pterygium seldom causes problems, it is uncommonly reported by participants (n = 52 self-reported pterygium). Cataracts were also uncommonly reported (n = 13) possibly because their occurrence is largely a feature of an older age group than studied here. Interestingly, sunburn history remained associated with higher damage even after adjustment for cumulative UV exposure, suggesting that high intensity intermittent sun exposure was also important.

Conclusion

Silicone casts of the skin in a sun-exposed area (here the dorsum of the hand) provide a simple, objective measure of cumulative UVR exposure for use in population-based epidemiologic research. Sun exposure during the early years of life may be particularly relevant to the measured skin damage, but there is also an association with sun exposure across the whole of life. The silicone cast measure of skin damage is particularly suitable where the interest is in sun exposure over the life course; in this situation, this is a relatively simple, rapid, and direct objective measure, which is easily graded with a high level of consistency. It can be used as an adjunct to other methods of sun exposure measurement, such as self-report using a calendar. However, for the latter, both completion and preparation of the data for analyses are time-consuming and complex. The appropriate tool is dependent on the

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research question: for example, in examination of health outcomes in relation to sun exposure over the whole of life, silicone casts may be preferred. On the contrary, if the aim is to examine the effect of sun exposure at specific ages (e.g., before age 10 years), then questionnaire methods such as the personal work and residence calendar will be more suitable (34).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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