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SUN EXPOSURE AND INTERACTION WITH FAMILY HISTORY IN RISK OF MELANOMA, QUEENSLAND, AUSTRALIA

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Sun exposure is the main environmental risk factor for melanoma, but the timing of exposure during life that confers increased risk is controversial. Here we provide the first report of the association between lifetime and age-specific cumulative ultraviolet exposure and cutaneous melanoma in Queensland, Australia, an area of high solar radiation, and examine the association separately for families at high, intermediate and low familial melanoma risk. Subjects were a population-based sample of melanoma cases diagnosed and registered in Queensland between 1982 and 1990 and their relatives. The analysis included 1,263 cases and relatives with confirmed cutaneous melanoma and 3,111 first-degree relatives without melanoma as controls. Data on lifetime residence and sun exposure, family history and other melanoma risk factors were collected by a mailed questionnaire. Using conditional multiple logistic regression with stratification by family, cumulative sun exposure in childhood and in adulthood after age 20 was significantly associated with melanoma, with estimated relative risks of 1.15 per 5,000 minimal erythemal doses (MEDs) from age 5 to 12 years, and 1.52 per 5 MEDs/day from age 20. There was no association with sun exposure in families at high familial melanoma risk. History of nonmelanoma skin cancer (relative risk [RR] = 1.26) and multiple sunburns (RR = 1.31) were significant risk factors. These findings indicate that sun exposure in childhood and in adulthood are important determinants of melanoma but not in those rare families with high melanoma susceptibility, in which genetic factors are likely to be more important.
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Key words: *melanoma; aetiology; ultraviolet radiation; family history*

Over the last 25 years, cutaneous melanoma has become an increasingly common cause of cancer morbidity and mortality in white-skinned populations world-wide.[1–3] Queensland, Australia, a tropical and subtropical area inhabited by persons of largely European descent, has the world's highest recorded incidence of this disease, with a lifetime risk of invasive melanoma in 1997 of 1 in 16 for men and 1 in 24 for women.[4] Melanoma incidence is also increasing[2,3,5] and has become a significant public health problem in regions at higher latitudes. In 1996 there were an estimated 7,761 new cases and 1,509 deaths from melanoma in the United Kingdom[6] and 38,300 new cases and 7,300 deaths in the United States.[7]

The aetiology of cutaneous melanoma is incompletely understood. Exposure to solar ultraviolet (UV) radiation is the major environmental risk factor[8] and the presence of large numbers of naevi and other host factors including skin pigmentation and sensitivity to the sun are also strongly associated.[9] Certain rare families carry germline mutations that confer extremely high disease susceptibility at an early age, although few of the genes involved in familial melanoma have been identified, and such families account for a small proportion of the total case burden.[10]

Although exposure to sunlight is one of the most important factors in melanoma pathogenesis, the timing of exposure during life and the amount of exposure that confers increased risk remain controversial. Confounding by constitutional factors is difficult to exclude. Exposure to high ambient UV radiation in early life appears to increase risk of melanoma in adulthood, but again, studies are inconsistent.[11]

This is the first report of the association between cumulative lifetime and age-specific UV exposure and cutaneous melanoma in a southern hemisphere population residing in an area of high ambient solar radiation. We describe the association between melanoma and cumulative UV exposure in childhood, adolescence and adulthood while accounting for the effect of known constitutional and familial risk factors and examine this association separately for members of high, intermediate and low melanoma risk families.

MATERIAL AND METHODS

Subjects

Subjects were a population-based sample of melanoma patients and their relatives selected for the Queensland Familial Melanoma Project, as described fully elsewhere.[12] Briefly, a one-page questionnaire about family history of melanoma was sent to all 10,407 Queensland residents with a histologically confirmed first primary cutaneous melanoma (either *in situ* or invasive) diagnosed in Queensland between January 1, 1982 and December 31, 1990 and registered with the Queensland Cancer Registry, and for whom doctor's permission to approach had been obtained. Of 7,784 (75%) respondents who agreed to be approached again, all who reported a parent, sibling or child with a history of melanoma (n = 1,529), a 20% sample of those who reported no such family history (n = 1,246) and all twins (n = 145) were selected for the study, a total of 2,920 patients. Relatives were ascertained according to a sequential sampling procedure.[13] All reported first-degree relatives of the selected patients were included in the study and if any of their relatives had a confirmed cutaneous melanoma, then their first-degree relatives were also included, and so on.

"Cases" were defined as the selected patients and all relatives of those patients with confirmed cutaneous melanoma, selected according to the above procedure, who returned usable questionnaires. "Controls" comprised all of the cases' first-degree relatives with no history of melanoma who were included in the study by returning usable questionnaires.

Data collection

A self-administered questionnaire was mailed to the 2,920 selected patients assessing standard melanoma risk factors, demographic and medical details, lifetime residence and sun exposure history to date and family history of melanoma.[12] The same questionnaire was mailed to all living first-degree relatives with a confirmed history of melanoma. A similar questionnaire, but not inquiring about family history, was mailed to all living first-degree relatives aged between 18 and 75 years who did not have a history of melanoma, for whom the case or other relatives provided name

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and contact address. Information on all risk factors used in the analysis was collected in identical fashion in cases and controls. In total, questionnaires were posted to 7,619 relatives of the selected patients. Data collection was carried out between 1990 and 1994.

Variables for analysis

Age in the analysis was defined for cases as age at diagnosis of melanoma and for controls as age at completion of the questionnaire.

Skin colour assessed on unexposed sites such as the inner upper arm was recorded in three categories (olive, medium, fair), eye colour in three categories (blue/grey, green/hazel, brown) and early adult hair colour in five categories (dark brown/black, fair/blonde, light brown, light red/ginger, dark red/auburn). Propensity to burn in the sun was categorised as "always burns" or other and tanning ability after prolonged sun exposure as "slight or no tan" or other. Naevus density was recorded in four categories by comparison with diagrammatic representations (none, few, moderate or many) and density of freckling in summer was categorised as none, $\leq$100 freckles or $>$100. Number of sunburns during life was grouped as $\leq$5 or $>$5.

Cumulative lifetime UV exposure. A lifetime residence calendar asked in which town and state or country subjects had resided when aged 0–4 years (preschool), 5–12 years (primary school), 13–19 years (adolescence), 20–29 years and during each subsequent decade of life, and what proportion of the day during that period was spent in the sun. Additional questions about the proportions of weekdays and weekend days spent outdoors and whether the main job or activity in each period occurred outdoors, indoors, or both were added to a later version of the questionnaire, which was received by about 45% of subjects.

For Australian places of residence an average annual UV flux was assigned from tables prepared by Paltridge and Barton.[14] Localities outside Australia were assigned UV values calculated by Whiteman.[15] For periods spent in the armed forces, an average value was calculated from the experience of Australian ex-serviceman.[16] Missing UV values due to gaps in the residential record were filled by inspection of the original questionnaire or by interpolation. Cumulative age-specific and adult UV doses from age 20 years were computed by multiplying the average annual UV flux in each life period by the reported proportion of time spent outdoors during that period and summing to index age, taking the different period lengths into account and interpolating where necessary. Cumulative exposure was expressed in terms of minimal erythemal dose (MED).[17] Five MEDs are roughly equivalent to an hour of exposure to the midday sun on a cloudless midsummer day in Australia.[18]

In over half the subjects the proportion of time spent outdoors was imputed for one or more periods by regression on the values for that subject's neighbouring periods, or otherwise from the average value for all subjects with complete responses who claimed mainly outdoor, partially outdoor or mainly indoor activities during the period. These procedures were undertaken in ignorance of subjects' melanoma status.

Childhood and adolescent UV exposure. Separate questions were asked about hours spent in the sun in summer on weekdays, weekend days and annual holidays between 9 am and 3 pm from ages 5–12 years and from 13–19 years. Solar radiation during these 6 hours accounts for about 75% of the total daily UV dose.[19] Each subject's annual total hours of exposure was calculated assuming a 6-week summer holiday and taking the responses to apply to the entire year. (Although the question referred only to summer, over much of Australia and especially in Queensland, winters are mild and the UV flux is substantial;[19] thus to neglect winter exposure would introduce greater inaccuracy than confining the calculation to summer.) The cumulative UV doses for these two periods were again computed by multiplying the average annual UV flux for the place of residence by the total hours of exposure in each period. In calculating exposure, these values, termed "childhood exposure" and "adolescent exposure," were used in place of the exposures calculated from the residence calendar for the same periods as they were more specific and the questions were more completely answered.

History of nonmelanoma skin cancer. Subjects reported their histories of treated nonmelanoma skin cancer (either basal cell [BCC] or squamous cell carcinoma [SCC]) and the year in which they were first diagnosed. A single variable was derived indicating the presence/absence of a history of BCC or SCC up to the age of completion of the questionnaire for controls and up to the age of first diagnosis of melanoma for cases. Nonmelanoma skin cancers with unreported dates of diagnosis (15% for both cases and controls) were disregarded for cases but included for controls: all reported events among controls must of necessity have occurred prior to questionnaire completion at enrollment, whereas 17% of nonmelanoma skin cancers were reported after the diagnosis of melanoma by cases. Since lesions with unknown dates could have occurred after index age in this group, omission is the appropriate conservative procedure.

Statistical analysis

The analytic approach used was conditional multiple logistic regression. Analyses were stratified in two ways. First, to account for genetic or familial similarity in sun exposure and personal characteristics, a conditional logistic regression was performed within strata defined by family affiliation. In this analysis, age was entered as a linear and a quadratic in age minus 40 years and average daily sun exposure after age 20 years was used, *i.e.*, cumulative exposure from age 20 years divided by the number of days since age 20. Only families with at least one member with melanoma and at least one member without melanoma in the final dataset were included in these analyses. Second, a conditional logistic regression was performed in which the strata were defined by age in years, and cumulative rather than average daily adult UV exposure was used. Analyses with stratification by family and by age were also performed separately for families at low, intermediate and high familial melanoma risk, defined in previous work by the degree to which the number of melanoma cases in a family exceeded or fell short of the number expected on the basis of population incidence rates and the family members' sexes, ages and birth cohorts.[20] All logistic analyses used the PHREG procedure in the SAS statistical package.[21]

All initial models also included childhood (5–12 years) and adolescent (13–19 years) UV exposure calculated as described above, history of nonmelanoma skin cancer, history of sunburn and constitutional risk factors (skin colour, eye colour, hair colour, propensity to burn in the sun, tanning ability, naevus density and freckling density). Skin colour and naevus density were included as quantitative scores with weights conforming approximately to the relative sizes of the logistic regression coefficients in preliminary analyses. The other variables were entered as indicator variables.

Preliminary multivariate analysis established that most of the predictive power in the set of constitutional risk factors listed above resided in skin and hair colour, propensity to burn in the sun and naevus density. Slightly less than 1% of subjects had missing values for the first three of these variables or for history of sunburn, and these missing values were imputed using SOLAS software,[22] sorted in each case on the five most closely related variables from among age, sex, year of birth and the other personal risk factors. Naevus density was missing for 6.5% of subjects. As this is one of the strongest risk factors for melanoma and is only weakly associated with other personal characteristics, imputation of missing values was considered not appropriate.

In order to include otherwise eligible individuals with missing naevus densities, two linear functions of personal risk factors were constructed with coefficients derived from preliminary analyses. In the first, the factors included were skin colour, hair colour, propensity to burn in the sun and naevus density; the second included,

in place of naevus density, tanning ability and eye colour. If naevus density had been recorded the first function was included; if not, the second function was employed.

Approximate attributable risks (ARs)[23] were computed from the case series, using the estimates of relative risk of melanoma for UV exposure in childhood and after age 20 years and for history of nonmelanoma skin cancer and history of sunburn. Confidence intervals were obtained by substituting lower and upper bounds of the respective relative risks in the computations, ignoring the variance arising from the distribution of the exposure factors. It can be shown that the latter component makes a negligible contribution if, as here, the case sample is large. In the case of the AR for childhood plus adult UV exposure, the asymptotic standard error of their sum weighted by the corresponding logistic coefficients, and an approximate confidence interval (CI), was computed in similar fashion.

RESULTS

Completed questionnaires were returned by 7,174 (68%) eligible subjects including 2,275 cases and 4,899 controls. Subjects younger than 20 years were excluded, as were subjects who had missing values for childhood and/or adult UV exposure, nonmelanoma skin cancer history and other risk factors (Fig. 1). This left 4,374 subjects, 1,263 cases and 3,111 controls with sufficient UV exposure and personal information for inclusion in multivariate analyses after imputation for some missing information as described above. Among these, 10 individuals with melanoma were in age strata without controls. Exclusion of deficient families reduced the sample size for the analysis within families to 3,080, comprising 987 cases and 2,093 controls.

Compared with the subjects excluded on grounds of inadequate information on sun exposure or nonmelanoma skin cancer, the included subjects had broadly similar distributions of hair and eye colour, propensity to burn, tanning ability and naevus density but had reportedly experienced more sunburns and tended to have fairer skin colour and more freckles. Cases and controls were similar in this respect. Among controls the mean ages were near 45 years of age in both included and excluded subjects, whereas the cases who were excluded were, at 53 years of age, almost 5 years older than those included. The proportion of females was similar in both groups. As anticipated, there was far more missing information on all personal characteristics, other than age and sex, among the excluded subjects. Distributions of cumulative childhood UV exposure, average UV exposure since age 20 years, history of sunburn and of nonmelanoma skin cancer and certain constitutional factors in cases and controls are given in Table I.

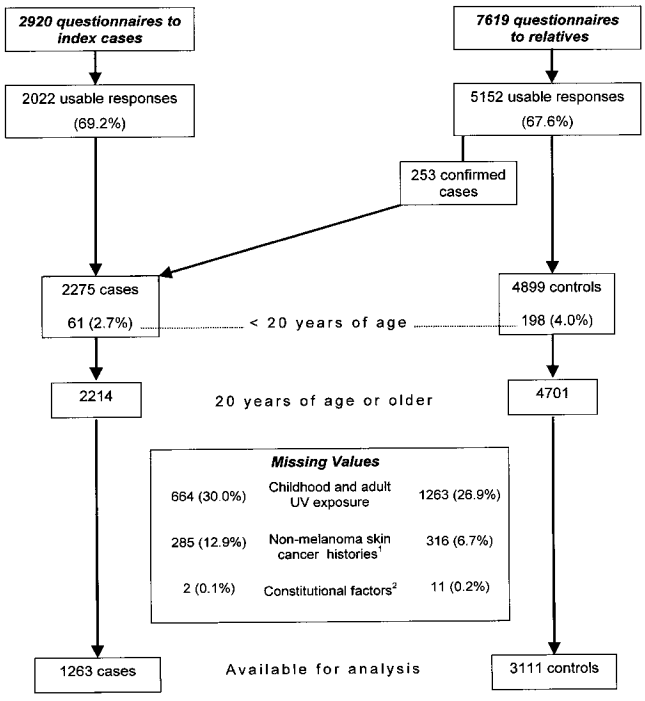

FIGURE 1 – Flow chart of responses to questionnaires and losses due to missing values. [1]Among subjects with known sun exposure.–[2]Among subjects with known sun exposure and nonmelanoma skin cancer histories. UV, ultraviolet.

There was a high correlation between age and year of birth (0.95 in cases, 0.99 in controls) due to the relatively short interval over which diagnoses of melanoma and enrollment of controls took place. Thus the effect of year of birth independent of age was impossible to determine.

Adolescent exposure had no predictive power in the presence of the childhood exposure variable. In the absence of the childhood exposure variable, adolescent exposure had significant influence on melanoma risk only when the adult sun exposure variable was also absent.

In both models, self-reported sun exposure, particularly in childhood but also after 20 years of age, was associated with the development of melanoma, as was a history of nonmelanoma skin cancer and multiple sunburns (Table II).When estimated within strata defined by family, relative risks were elevated for both childhood sun exposure (odds ratio [OR] = 1.15 per 5,000 MEDs from age 5 to 12 years) and average daily adult sun exposure (OR = 1.52 per 5 MEDs/day from age 20 years); the former value was somewhat higher than that estimated within strata of age (Table II). Estimates for nonmelanoma skin cancer and sunburn histories were similar for both models and indicated an approximate 30% increase in risk of melanoma associated with the presence of either factor.

When the analyses were repeated within groups defined as high, intermediate and low familial melanoma risk, there was significant heterogeneity in odds ratios for childhood sun exposure, with odds ratios significantly elevated in the lowest familial risk strata but below unity in the highest risk strata (Table III). For adult UV exposure, there was a weaker and nonsignificant trend in the same direction. After adjustment for sun exposure, sex and site of lesion,

TABLE I – DISTRIBUTIONS OF RISK FACTORS AMONG CASES AND CONTROLS[1]

	Cases		Controls	
	Median	IQR	Median	IQR
Childhood UV[2]	2.2	1.1–2.8	1.9	1.1–2.8
Average cumulative UV dose since age 20 years[3]	0.7	0.4–1.0	0.6	0.3–0.9
Skin type		*n* (%)		*n* (%)
Always burn		196 (15.5)		307 (9.9)
Tanning ability				
Slight or no tan		582 (46.5)		1108 (35.8)
Skin color				
Fair		928 (73.5)		1988 (63.9)
Medium		298 (23.6)		959 (30.8)
Hair color				
Blond/light brown		671 (58.5)		1341 (57.2)
Light or dark red		157 (13.8)		199 (8.5)
Eye color				
Brown		206 (16.6)		638 (22.1)
Nevus numbers				
Moderate or many		415 (43.2)		885 (30.0)
Sunburn history				
At least 6		477 (37.8)		944 (30.2)

[1]IQR, interquartile range; UV, ultraviolet. –[2]5,000 MEDs from ages 5 to 12 years.–[3]5 MEDs per day.

TABLE II – ODDS RATIOS (OR) FOR MELANOMA, ATTRIBUTABLE RISKS (AR) AND 95% CONFIDENCE INTERVALS (CI) FOR CHILDHOOD SUN EXPOSURE, CUMULATIVE ADULT SUN EXPOSURE AND HISTORY OF NONMELANOMA SKIN CANCER AND SUNBURNS

	Adjusted OR[1]	95% CI	AR (%)	95% CI
Analysis within family strata, adjusted for age				
Childhood sun exposure[2]	1.15	1.07–1.25	25.2	13.0–36.8
Average daily sun exposure since age 20 years[3]	1.52	1.27–1.83	26.1	15.8–34.7
Nonmelanoma skin cancer before or at diagnosis/enrollment	1.26	1.02–1.55	6.8	0.7–11.8
Six or more sunburns	1.31	1.08–1.58	9.1	2.8–14.3
Childhood and adult exposure			44.3	32.1–53.9
Analysis within strata of age				
Childhood sun exposure[2]	1.10	1.03–1.16	17.9	6.7–27.3
Cumulative sun exposure since age 20 years[4]	1.02	1.01–1.03	15.8	7.4–22.7
Nonmelanoma skin cancer before or at diagnosis/enrollment	1.35	1.14–1.59	8.7	4.2–12.4
Six or more sunburns	1.25	1.08–1.45	7.7	2.8–11.8
Childhood and adult exposure			30.6	19.3–39.9

[1]Conditional logistic regression analysis adjusted for skin colour, hair colour, propensity to burn in the sun, naevus density and all other terms listed in the model.–[2]Per 5,000 minimum erythemal doses (MEDs) from ages 5–12 years.–[3]Per 5 MEDs per day on average since age 20.–[4]Per 5,000 MEDs since age 20.

TABLE III – ODDS RATIOS (OR) FOR MELANOMA FOR CHILDHOOD SUN EXPOSURE, CUMULATIVE ADULT SUN EXPOSURE AND HISTORY OF NONMELANOMA SKIN CANCER AND SUNBURNS, ACCORDING TO FAMILIAL MELANOMA RISK

	Adjusted OR[1] according to familial melanoma risk			Test for homogeneity χ^2 (2 df)	*p*-value
	High	Medium	Low		
Analysis within family strata, adjusted for age					
Childhood sun exposure[2]	0.97	1.01	1.29	9.10	<0.05
Average daily sun exposure since age 20 years[3]	0.95	1.55	1.58	2.26	
Nonmelanoma skin cancer before or at diagnosis/enrollment	1.42	1.24	1.27	0.11	
Six or more sunburns	0.92	1.33	1.33	0.89	
Analysis within strata of age					
Childhood sun exposure[2]	0.86	0.99	1.14	6.56	<0.05
Cumulative sun exposure since age 20 years[4]	1.01	1.02	1.03	0.55	
Nonmelanoma skin cancer before or at diagnosis/enrollment	1.64	1.26	1.38	0.53	
Six or more sunburns	0.57	1.37	1.32	6.05	<0.05

[1]Conditional logistic regression analysis adjusted for skin colour, hair colour, propensity to burn in the sun, naevus density and all other listed terms in the model.–[2]Per 5,000 MEDs from ages 5–12 years.–[3]Per 5 MEDs per day on average since age 20.–[4]Per 5,000 MEDs since age 20.

the mean ages at diagnosis in the high risk group was 46.8 years, compared with 47.7 and 49.2 years in the intermediate and low risk groups, respectively. The largest differences were observed in subjects with face and lower limb lesions.

The estimates of attributable risk were consistently largest for childhood and adult UV exposure, reaching 44% for the combination of these two factors in the analysis within family strata (Table II). Estimates from this analysis have appreciably wider confidence intervals. Attributable risks for the skin cancer and sunburn variables were similar to each other and comparable between the models (Table II). The combination of all four factors (childhood exposure, adult exposure, history of nonmelanoma skin cancer, history of sunburn) added approximately 10% to the estimated attributable risk for combined childhood and adult sun exposure.

DISCUSSION

Our data indicate that measures of cumulative sun exposure in childhood and adulthood are strongly associated with the subsequent development of melanoma overall, although not within families with high melanoma susceptibility. From the estimates of attributable risk it appears that in persons without genetic susceptibility, these two factors are major determinants of melanoma risk. Together with the two other sun-related factors, nonmelanoma skin cancers and multiple sunburns, the population attributable risk is estimated to exceed 50%. As in all observational studies reliant on self-report, issues of bias need to be addressed, particularly selection and recall bias.

Selection bias is a possibility but is unlikely to be of great importance. Ascertainment of subjects with a history of melanoma was estimated to be virtually complete.[12] All eligible melanoma patients who reported a family history were enrolled in the study, and the others were sampled at random. All reported living relatives were contacted. There was further selection of both cases and controls on the basis of availability of information on sun exposure or nonmelanoma skin cancer, but, as reported above, this appeared to be nondifferential. However, atypical distributions of UV exposure in cases (and equally in controls) arising from nondifferential selection (due to, for instance, availability of information) could affect the estimates of population attributable risk to some degree. In addition, the case series has a somewhat higher proportion of

familial cases than in the population, which would tend to bias the attributable risks for UV exposure downward.

Wide publicity has long been given in Australia to the role of sun exposure in the development of skin cancers of all sorts; it would not be surprising if persons with a history of melanoma tended to overstate the amount of time they recalled spending in the sun both in childhood and subsequently. Some indication of the magnitude of the bias can be obtained from considering the variable recording whether the main activity at each stage or decade of life was mainly indoors, mainly outdoors or mixed; this question was only posed in the final version of the questionnaire. With only three options, the potential for biased response is more limited. In each decade of life from 20 years of age onwards we computed for cases and controls the mean reported fraction of time spent outdoors corresponding to each option. Although this mean was sometimes lower in cases than controls for the "mainly outdoors" category (about 16% of responses), it was always greater in cases for the other categories and averaged out at approximately 5% higher overall. However, when the childhood and adolescent cumulative exposure variables were subjected to the same analysis, the difference between cases and controls was much less, the fraction of time spent outdoors in cases averaging out at only 1% greater than in controls. Moreover, the absence of an elevated odds ratio for adult exposure among families classified as at high familial risk and for childhood exposure in those classified as at high and medium familial risk argues against the presence of substantial recall bias.

Incomplete control of confounding may also act to exaggerate the effect of the various measures of sun exposure. Inclusion of omitted personal characteristics such as eye colour or ability to tan had no appreciable effect on the relative risks for childhood and adult UV exposure and for nonmelanoma skin cancer and sunburn, nor did inclusion of the characteristics individually. Nonetheless, it remains possible that fuller information on potential confounders would reduce the relative and attributable risks of sun exposure. On the other hand, the misclassification of sun exposure that is undoubtedly present would serve to weaken estimates of its association with melanoma risk. Cases were asked to recall age-specific exposures and other events that were 5 or 6 yr earlier than controls of the same age. This might introduce some additional imprecision, but there is no reason to think that it would induce bias. Thus, although it is possible that the attributable risks have been overestimated to some degree, it is unlikely that the findings related to cumulative UV exposure are entirely due to bias or chance.

With regard to the increased melanoma risk associated with a prior diagnosis of nonmelanoma skin cancer (NMSC), caution is necessary. Not only is a degree of selective recall possible, but some respondents may have interpreted the question as referring to their melanomas, although among cases, the proportion of reported NMSC diagnoses occurring within a year of the melanoma diagnosis (26%) is only slightly higher than the proportion of controls reporting NMSC diagnoses within a year of enrollment (23%). On the other hand, NMSCs with no reported year of diagnosis were rejected among cases only, which would tend to bias results in the null direction.

From the point of view of data analysis, the model with stratification by family affiliation mirrors most closely the design structure of the study and is in this sense the most valid. It controls for any additional correlation between family members in constitutional and other risk factors, beyond that accounted for by the other terms in the model (skin colour, hair colour, propensity to burn and naevus density). Thus, estimates of increased risk from this model provide the best indication of the overall effect of UV exposure, independent of familial factors. On the other hand, the adult exposure variable is computed up to the year of index age, resulting in a close relationship between these two variables. Stratification by age may in consequence be superior in measuring the effect of cumulative adult UV exposure, and this model produces smaller standard errors. It is reassuring that both models give qualitatively similar results in terms of attributable risks.

Our findings of increased risk of melanoma associated with childhood sun exposure are consistent with studies of melanoma incidence in fair-skinned migrants from areas of low to areas of high insolation that demonstrate an increased risk in persons who experience high ambient UV exposure in childhood.[11] Our results also indicate significant interaction between the effect of sun exposure on melanoma risk and familial susceptibility to melanoma. In this sample, as in other populations, melanoma in highly susceptible families occurs at a younger age on average than in the population at large (cf. ref. 20). This is consistent with the hypothesis that melanoma develops in a susceptible subset of the population who receive a threshold UV dose and that those with high genetic susceptibility have a lower threshold and reach this earlier than others in the same environment.[24] In an area of high solar radiation such as Queensland, most people achieve high levels of sun exposure early in life. Our results based on separate analyses within three levels of familial risk suggest that in such an environment, within high risk families, it is genetic factors rather than differences in sun exposure that determine who will get the disease. Within families at relatively low genetic risk, who comprise the majority of the population, cumulative sun exposure is likely to be a more important determinant of melanoma risk.

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