ORIGINAL ARTICLE

Sun exposure and risk of melanoma

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Background: As skin cancer education programmes directed to children and adolescents continue to expand, an epidemiological basis for these programmes is necessary to target efforts and plan for further evaluation.

Aims: To summarise the epidemiological evidence on sun exposure during childhood and adolescence and melanoma risk.

Methods: A literature review was conducted using Medline (1966 to December 2004) to identify articles relating to sun exposure and melanoma. The review was restricted to studies that included sun exposure information on subjects 18 years of age or younger.

Results: Migrant studies generally indicate an increased melanoma risk in individuals who spent childhood in sunny geographical locations, and decreasing melanoma risk with older age at arrival. Individuals who resided in geographical locations close to the equator or close to the coast during childhood and/or adolescence have an increased melanoma risk compared to those who lived at higher latitudes or never lived near the coast. The intermittent exposure hypothesis remains controversial; some studies indicate that children and adolescents who received intermittent sun exposure during vacation, recreation, or occupation are at increased melanoma risk as adults, but more recent studies suggest intermittent exposure to have a protective effect. The majority of sunburn studies suggest a positive association between early age sunburn and subsequent risk of melanoma.

Conclusion: Future research efforts should focus on: (1) clarifying the relation between sun exposure and melanoma; (2) conducting prospective studies; (3) assessing sun exposure during different time periods of life using a reliable and quantitative method; (4) obtaining information on protective measures; and (5) examining the interrelations between ability to tan, propensity to burn, skin type, history of sunburns, timing and pattern of sun exposure, number of nevi, and other host factors in the child and adolescent populations.

Despite the decreasing incidence and mortality for many types of cancer, the incidence rate for melanoma skin cancer has been rising in the United States since 1973.^{1,2} Melanoma is the most fatal of skin cancers accounting for 79% of all skin cancer deaths.³ The number of new melanomas that will be diagnosed in 2005 is estimated to be about 59 580 and it is predicted that there will be about 7770 deaths due to melanoma.² While melanoma is thought to be rare in individuals under the age of 20, recent evidence has indicated a rapidly rising incidence of melanoma in children and teenagers,^{4–7} and epidemiological studies have revealed a strong association between sun exposure during critical periods of early life and subsequent risk of melanoma during adulthood.^{8–16}

Although the effects of sun exposure during early life are thought to be important, there remains controversy about the age period when most of an individual's exposure occurs. Some studies have shown that most exposure occurs during childhood and adolescence.^{17–18} Children spend an estimated 2.5–3.0 hours outdoors each day^{19–21} and may receive three times more annual ultraviolet-B rays than adults because they have a greater opportunity for midday sun exposure during the summer months.^{17–22–23} Conversely, other studies have found that children receive the same amount of ultraviolet doses as adults because the recent technological revolution of the 1990s and advent of various electronic games and computers gave children and adolescents more incentive to stay indoors during the day.^{24–25} In either case, health behaviours and habits that are established in childhood, including unprotected sun exposure, may be sustained into adulthood.^{18–22–26–34} As skin cancer education programmes directed to children and adolescents continue to expand, an

epidemiological basis for these programmes is necessary to target efforts and plan for further evaluation. The purpose of this review is to summarise the epidemiological evidence on sun exposure during childhood and adolescence and risk of melanoma in order to more effectively target public health programmes.

METHODS

Literature search

We conducted a computerised literature search of the Medline database of the National Library of Medicine for the time period 1966 to December 2004 and limited the scope of our search to those studies published in English. We conducted our search using the following MeSH headings: adolescent, child, melanoma, skin neoplasms, sunburn, sunlight, and ultraviolet rays. We further reviewed the reference lists of relevant book chapters and obtained printed materials from recent scientific meetings addressing this topic.

The review was restricted to studies that included sun exposure information on subjects 18 years of age or younger. Studies identified for inclusion were based on the following criteria: (1) assessed associations between sun exposure and melanoma; and/or (2) assessed associations between surrogate measures of sun exposure (such as place of birth; duration of residence; sunburn history; and time spent on vacation, recreation, and outdoor activities) and melanoma. In some instances, relevant results were presented for age groups in the range 15–25 years; we critiqued these studies and included them in our review.

We classified studies into three groups based on the existing literature and the common use of these surrogate

measures: (1) migration and geographical residence; (2) sun exposure including intermittent exposure; and (3) sunburn.

RESULTS

Migration and geographical residence studies

Migrant studies are commonly used to examine sun exposure and melanoma risk by comparing incidence in populations who have migrated between different geographical areas. Migrant studies provide compelling evidence of childhood and adolescence being critical times for future melanoma development, that is, an increased risk for individuals who spent childhood in sunny geographical locations.^{35–44} In a case-control study (511 cases and 511 controls) by Holman and Armstrong,³⁵ age at arrival and duration of residence in Australia was studied. Earlier age at arrival was a predictor of melanoma risk with little residual effect of duration of residence.^{35–45} Specifically, migrants arriving before age 10 years appeared to have a risk similar to that of native born Australians, whereas the estimated incidence in those arriving after age 15 years was around one quarter of the native born rate, with arrival at later ages giving no additional advantage.³⁵ In another analysis using these data, English and Armstrong⁴³ identified people at high risk of cutaneous melanoma. Age ≥ 10 years old at arrival in Australia was associated with a reduced risk of melanoma (OR = 0.38; 95% CI 0.24 to 0.61) compared to age at arrival < 10 years old. Similarly, in a case-control study (412 cases and 445 controls) involving patients from Germany, Belgium, and France, age < 10 years old at arrival in a sunny location of residence (that is, the Mediterranean, subtropics, or tropics) conferred a fourfold increased risk of developing melanoma.³⁸

In a review by Whiteman and Whiteman,¹⁴ migrant studies were classified based on three criteria: (1) place of birth; (2) age at migration; and (3) duration of residence. Place of birth studies showed that melanoma rates among migrants born in areas of low insolation (i.e. Northern Europe) migrating to areas of high insolation (i.e. Israel and Australia) were lower than natives born at the high insolation area.^{39–42–44–46–52} Two studies reported an opposite effect, that is, higher melanoma risk among low insolation born migrants (i.e. Europe) migrating to high insolation areas (i.e. Hawaii, Israel) than among natives of the high insolation country.^{53–54} Age at migration studies showed decreasing melanoma risk with older age at arrival when individuals migrated to a place close to the equator.^{35–39–44} Lastly, although choice of reference group varied, all 10 duration of residence studies reported increased melanoma risk with longer duration of residence in the adopted country.^{35–36–38–39–42–44–47–48–54–55}

In addition to migrant studies, location of residence studies provide further evidence that sun exposure in childhood and adolescence is closely associated with melanoma risk. Weinstock and colleagues⁴¹ conducted a nested case-control analysis involving 130 cases and 300 controls from the Nurses' Health Study cohort, and observed an increased risk of melanoma in women whose residence during the ages 15–20 years was more equatorial in latitude. On the other hand, these data also showed that latitude of residence after 30 years of age was not significantly related to melanoma risk. In another study of 474 cases and 926 controls, those who lived near the coast before the age of 15 years had an increased risk of melanoma compared to those who never lived near the coast (OR = 1.6; 95% CI 1.0 to 2.6).⁵⁶

Sun exposure

Intermittent exposure hypothesis

Epidemiological studies suggest, based on the “intermittent exposure hypothesis”, that periodic versus long continued heavy sun exposure is the most important in melanoma

causation.^{10–57–61} Elwood⁵⁷ has defined intermittent sun exposure as that usually received during recreational and vacation activities. It has been put forth that chronic or “regular” sun exposure may actually reduce the risk of melanoma.^{51–60–63} However, in epidemiological studies the intermittent exposure hypothesis has caused much controversy. For example, the 10 duration of residence studies^{35–36–38–39–42–44–47–48–54–55} reported an increased melanoma risk with longer duration of residence in the adopted country, suggesting that chronic sun exposure may be an important factor in melanoma development. While duration of residence studies are crude measures of sun exposure, they are easy to classify and there is evidence that they can be a reasonable proxy for sun exposure when comparing populations.^{14–64} Thus, past studies have indicated that intermittent sun exposure is associated with increased risk for melanoma, and more recent studies have reported that factors associated with high levels of sun exposure, such as elastosis,^{65–66} sunburn, and intermittent sun exposure, may increase survival from melanoma.⁶⁷

Different biological events may result from acute, intense sun exposure as opposed to high dose chronic sun exposure. An intermittent pattern of exposure causes DNA damage to melanocytes which eventually may lead to the development of melanoma.¹³ In the model proposed by Gilchrest and colleagues,¹³ when melanocytes are damaged by intermittent intense ultraviolet radiation in the presence of both low melanin content (which has a photoprotective role in the skin) and low basal DNA repair capacity, they are likely to survive. This low DNA repair capacity in conjunction with the retention of “damaged” cells may increase the risk of melanoma. Cells may be at their highest vulnerability for genomic damage from intermittent sun exposures during childhood and adolescence.¹³

Sun exposure during vacation, recreation, and occupation

Sun exposure during vacation, recreation, or occupation may reflect intense intermittent exposure. Several studies ($n = 11$) have looked at time spent in sunny vacations, specific types of recreational activities, or occupation during childhood or adolescence and risk of melanoma^{36–45–52–60–62–68–72} (see table 1). There is conflicting evidence: while some studies have determined that intermittent sun exposure during this critical time period leads to an increased melanoma risk, others have not. The exceptions are: (1) a German case-control study of 271 matched pairs which determined that outdoor activities in childhood have a protective effect with an odds ratio of 0.3 (95% CI 0.1 to 1.1);⁷² (2) an Australian case-control study of 507 matched pairs that showed when recreational sun exposure was expressed as a proportion of total outdoor exposure, the association between melanoma and intermittent exposure was not supported;⁴⁵ (3) a US case-control study of 130 cases and 300 controls which determined that among sun resistant women (women who tend to tan readily instead of burn when exposed to sun), aged 15–20 years, high frequency of swimsuit use appeared to be protective against melanoma risk with an odds ratio of 0.3 (95% CI 0.1 to 1.0);⁶⁹ (4) a US case-control study of 256 cases and 273 controls in which deep/moderate tanners appeared to be protected from melanoma with increasing sun exposure at ages 2–10 years (OR = 0.30, 95% CI 0.17 to 0.55) and at ages 11–20 years (OR = 0.31, 95% CI 0.16 to 0.59);⁶² and (5) a Canadian case-control study of 583 cases and 608 controls which showed that melanoma risk was significantly reduced in those who were positive for the indicators of sun exposure based on days of outdoor activity at ages 10–12 years (OR = 0.67, 95% CI 0.52 to 0.85).⁶¹

Table 1 Summary of results from studies on recreation, vacation, and/or occupation sun exposure during childhood and adolescence and melanoma skin cancer

First author (reference), year, location	Study design No. cases/ controls	Assessment of sun exposure and comparison	Critical age periods investigated	RR/OR (95% CI)	Adjusted RR/OR (95% CI)	Comments
Recreation, vacation, and/or occupation						
Paffenbarger, ⁵² 1978, USA	Retrospective cohort 45/180	Outdoor employment (yes v no)	Prior to college	3.9 (N/A)	N/A	Purpose of study to generate hypotheses
Lew, ⁶⁸ 1983, USA	Case-control 111/107	Length of vacation in sunny places (≥30 days v <28 days)	Childhood	2.5 (1.1–5.8)	N/A	No adjustment for confounders
Green, ³⁶ 1986, Australia	Case-control 153/154	Total hours of sun exposure (≥5000 v <500)	Childhood Adolescence (age 10–19 y)	1.8 (N/A)	4.4 (1.8–184.5)	Adjusted for age and nevi
Holman, ⁴⁵ 1986, Australia	Case-control 507/507	Outdoor exposure proportion (≥60% v <29%)	Childhood Adolescence (age 10–24 y)	N/A	1.57 (0.87–2.83)	Limited to SSM; adjusted for acute, chronic skin reaction, hair colour, origin, and age at arrival
Weinstock, ⁶⁹ 1991, USA	Nested case-control 130/300	Swimsuit use outdoors (most v least frequent use)	Adolescence (age 15–20 y)	N/A	3.5 (1.3–9.3) (sun-sensitive) 0.3 (0.1–0.8) (sun-resistant)	Adjusted for age, sun sensitivity, and latitude of residence
Zanetti, ⁷⁰ 1992, Italy	Case-control 260/416	Beach holidays (1–59 weeks v zero)	Childhood	N/A	2.8 (1.6–4.6)	Adjusted for sex and age
Nelemans, ⁶⁰ 1993, Netherlands	Case-control 141/183	Sunbathing (yes v no)	Adolescence (age 15–25 y)	N/A	3.00 (1.43–6.30) (indoor worker) 0.76 (0.32–1.80) (outdoor worker)	Adjusted for age, sex, education, tendency to burn, hair colour, and freckling. Effect modification apparent: increased risk in sun sensitive individuals
Nelemans, ⁶⁰ 1993, Netherlands	Case-control 141/183	Water sports (yes v no)	Adolescence (age 15–25 y)	N/A	2.20 (0.75–6.49) (indoor worker) 2.61 (0.65–10.49) (outdoor worker)	Adjusted for age, sex, education, tendency to burn, hair colour, and, freckling. Effect modification apparent: increased risk in sun sensitive individuals
Nelemans, ⁶⁰ 1993, Netherlands	Case-control 141/183	Vacations in sunny countries (yes v no)	Adolescence (age 15–25 y)	N/A	2.44 (1.09–5.42) (indoor worker) 0.77 (0.31–1.93) (outdoor worker)	Adjusted for age, sex, education, tendency to burn, hair colour, and, freckling. Effect modification apparent: increased risk in sun sensitive individuals
White, ⁶² 1994, USA	Case-control 256/273	Sun exposure index (based on days of sun exposure and amount of clothing worn for protection) high v low	Childhood (age 2–10 y) Adolescence (age 11–20 y)	N/A	0.30 (0.17–0.55) (childhood) 0.31 (0.16–0.59) (adolescence)	Limited to “deep/moderate tanners”; adjusted for age, sex, and education; dose response effect
Nelemans, ⁷¹ 1994, Netherlands	Case-control 128/168	Swimming pools v none	Childhood Adolescence (age <15 y)	3.11 (1.66–5.75) (swimming pools)	2.20 (1.05–4.62) (swimming pools)	Adjusted for age, gender, education, hair colour, freckling, tendency to burn, and sunlight exposure
		Open waters v none		2.24 (1.11–4.52) (open waters)	2.41 (1.04–5.58) (open waters)	
Walter, ⁶¹ 1999, Canada	Case-control 583/608	Days of outdoor activity (>100 v ≥100)	Adolescence (age 10–20 y)	0.67 (0.53–0.85)	0.67 (0.52–0.85)	Adjusted for age, gender, and skin reaction to sun
Walter, ⁶¹ 1999, Canada	Case-control 583/608	Beach vacations (yes v no)	Age 12 y	1.63 (1.29–2.07)	1.67 (1.31–2.12)	Adjusted for age, gender, and skin reaction to sun
			Age 18 y	1.26 (0.98–1.63)	1.29 (1.00–1.67)	
Kaskel, ⁷² 2001, Germany	Case-control 271/271	Outdoor activities (at least one of walking, playing soccer, cycling, athletics, or gardening v none)	Childhood (age ≤12 y)	N/A	0.3 (0.1–1.1)	Adjusted for age, gender and residence

Although there is an abundance of epidemiological studies relating to the intermittent exposure hypothesis, such studies have been hampered by the lack of a precise definition which can be operationalised. Epidemiological studies to date have focused on sunburn history as a surrogate measure of intermittent exposure during childhood and adolescence. Sunburn is the result of overexposure to the sun without adequate sun protection and thus can be considered a measure of intermittent and/or intense sun exposure to unadapted or unadaptable skin.

Sunburn

Epidemiological studies support an age relationship between sunburn and melanoma. To date, there have been 17 case-control studies addressing the association between sunburn during *childhood* and melanoma^{56 68 70 72–85} (see table 2). It should be noted that the definition of sunburn varies across studies, ranging from the presence of any sunburn, to sunburns that are painful and or blistering. Elwood and Jopson¹⁰ presented an analysis of nine of these studies^{56 70 73–79} with summary odds ratio estimates. The overall summary

Table 2 Summary of results from studies on sunburn during childhood and adolescence and melanoma skin cancer

First author (reference), year, location	Study design No. cases/controls	Assessment of sun exposure	Critical age periods investigated	RR/OR (95% CI)	Adjusted RR/OR (95% CI)	Comments
Sunburn						
Lew, ⁴⁸ 1983, USA	Case-control 111/107	Painful sunburns (childhood) Blistering sunburns (adolescence) (yes v no)	Childhood Adolescence	N/A	2.8 (1.3–6.3) (childhood) 2.05 (1.18–3.56) (adolescence)	No adjustment for confounders; painful sunburn during childhood assessed in good tanners
Elwood, ⁷⁴ 1984, Canada	Case-control 595/595	Episodes of severe sunburn (severe/frequent v rare/mild)	Childhood	1.9 (N/A)	1.3 (0.9–1.8)	Adjusted for hair, skin/eye colour, freckles, sun reaction, and ethnicity
Holman, ⁷³ 1986, Australia	Case-control 507/507	≥ 5 painful sunburns v none	Childhood (age < 10 y) Adolescence (age 15–24 y)	N/A	1.11 (0.51–2.41) (childhood) 0.98 (0.53–1.82) (adolescence)	Limited to superficial spreading melanoma; adjusted for acute, chronic skin reaction, hair colour, country of origin, and age at arrival
Cristofolini, ⁸⁶ 1987, Italy	Case-control 103/205	Severe sunburn (yes v no)	Adolescence or early adult life	N/A	0.70 (0.41–1.19)	Adjustment for age and sex only
Østerlind, ⁵⁶ 1988, Denmark	Case-control 474/926	≥ 5 Painful (severe) sunburns v never	Childhood (age < 15 y) Adolescence (age 15–24 y)	3.7 (2.3–6.1) (childhood) 2.4 (1.6–3.6) (adolescence)	2.7 (1.6–4.8) (childhood) 1.9 (1.2–3.1) 1.2 (0.6–2.7)* (adolescence)	Adjusted for sex, number of nevi, freckles, and hair colour; dose response apparent
Weinstock, ⁴¹ 1989, USA	Nested case-control 130/300	≥ 5 Blistering sunburns v 0	Adolescence (age 15–20 y)	1.9 (1.1–3.4)	N/A	No adjustment for confounders
Elwood, ⁷⁵ 1990, UK	Case-control 195/195	Severe sunburn (ever v never)	Childhood (age 15–20 y)	N/A	2.4 (0.8–7.3)	Adjusted for nevi, freckling, social class, hair colour, and tendency to burn
Zanetti, ⁷⁰ 1992, Italy	Case-control 260/416	Sunburn (often) v never	Childhood (age 8–12 y)	12.0 (4.6–31.0) (sunburn often) 6.5 (3.4–12.3) (severe sunburn)	3.8 (2.3–6.4) (ever sunburn childhood)	Adjusted for sex, age, and type of skin reaction; dose response effect
Nelemans, ⁶⁰ 1993, Netherlands	Case-control 141/183	History of sunburn (yes v no)	Adolescence (age 15–25 y)	N/A	3.90 (1.82–8.33) (indoor worker) 1.90 (0.89–4.06) (outdoor worker)	Adjusted for age, sex, education, tendency to burn, hair colour, and freckling. Effect modification apparent: increased risk in sun sensitive individuals
Auriel, ⁷⁶ 1994, Belgium, France, Germany	Case-control 420/447	≥ 5 Painful sunburns	Childhood (age 5–14 y) Adolescence (> age 14 y)	1.75 (1.09–3.01) (childhood) 1.86 (1.19–2.46) (adolescence)	1.49 (0.97–2.32) (childhood)	Adjusted for hair/eye colour, ability to tan, nevi count, and density of freckles
Garbe, ⁸⁴ 1994, Germany	Case-control 513/498	No. of sunburns	Childhood and adolescence (age < 20 y)	N/A	N/A	Number of sunburns higher in cases
Westerdahl, ⁷⁷ 1994, Sweden	Case-control 400/640	> 5 Sunburns v never	Childhood (< age 15 y) Adolescence (age 15–19 y)	1.0 (0.5–2.1) (childhood) 0.9 (0.4–2.1) (adolescence)	1.6 (1.0–2.6) (childhood) 1.6 (1.0–2.5) (adolescence)	Adjusted for nevi and hair colour
Holly, ⁷⁸ 1995, USA	Case-control 452/930	Severe/frequent v rare/mild/no sunburn; ≥ 7 painful sunburns v none	Childhood (≤ age 12 y); elementary and high school	3.3 (2.3–4.7) (childhood) 2.0 (1.4–2.9) (elementary school) 2.4 (1.6–3.5) (high school)	1.9 (1.2–3.0) (childhood)	Adjusted for sunscreen use, skin reaction to sun, hair colour, nevi, complexion, ethnicity, history of skin cancer, and age; dose response apparent; effect modification by ability to tan
Ródenas, ⁷⁹ 1996, Spain	Case-control 105/138	Painful sunburn (often v never); blistering sunburn (yes v no); sunbaths (211 v 0)	Childhood (< age 15 y)	N/A	2.4 (1.1–5.52) (painful sunburn) 3.6 (1.5–8.4) (blistering sunburn) 5.5 (2.3–13.3) (sunbaths)	Adjusted for age, skin colour and type; dose response apparent
Pfahler, ⁸⁵ 2001, Europe	Case-control 603/627	≥ 6 sunburns v none	Childhood (≤ age 15 y)	N/A	2.0 (1.2–3.5)	Adjusted for location, ethnic origin, age and sex

Table 2 Continued

First author (reference), year, location	Study design No. cases/controls	Assessment of sun exposure	Critical age periods investigated	RR/OR (95% CI)	Adjusted RR/OR (95% CI)	Comments
Kaskel, ⁷² 2001, Germany	Case-control 271/271	Sunburn ever v never	Childhood (≤ 12 y)	5.7 (3.2–10.1)	1.9 (0.9–4.2)	Adjusted for age, gender, and residence
Siskind, ⁸⁰ 2002, Australia	Case-control 1263/3111	Hours in summer sun on weekdays, weekends and holidays	Childhood (age 5–12 y)	N/A	1.2 (1.1–1.3)	Adjusted for skin colour, hair colour, propensity to burn, nevus density, and age
Kennedy, ⁸⁵ 2003, Netherlands	Case-control 80/386	Painful sunburn	Childhood/adolescence (age 0–19 y)	N/A	1.4 (0.9–2.1)	Adjustment for age, sex, and skin type
Soloman, ⁸¹ 2004, USA	Case-control 386/727	No. of sunburns (3+ v none)	Female childhood (age 2–10 y) Female adolescence (age 11–20 y) Male childhood (age 2–10 y) Male adolescence (age 11–20 y)	N/A	3.4 (2.2–5.4) 3.3 (2.0–5.3) 1.8 (1.2–2.8)	Adjustment for age, sex, income, tendency to burn, and sunburns during age 2–10
Bataille, ⁸² 2004, UK	Case-control 413/416	Severity of sunburns (ever v never)	Childhood (< 15 y)	1.6 (1.1–2.3)	2.3 (1.4–3.5) 1.3 (0.9–2.0)	Adjusted for age, gender, and skin type

odds ratio based on nine of the published studies and a total of 2732 cases was 1.95 (95% CI 1.66 to 2.31). All of the studies reported an increased risk of melanoma with history of sunburn during childhood; odds ratios for individual studies ranged from 1.2 to 6.5. The lower bound of the majority of the confidence intervals presented for each study (6 of 9) was at or above the null value of 1.0, indicating the range of the true increased risk associated with sunburn history. Summary estimates were calculated for seven studies, excluding the two studies that were outliers based on tests of heterogeneity. The summary odds ratio was 1.62 (95% CI 1.35 to 1.95) based on 2010 cases.

Twelve case-control studies have addressed the association between sunburn during adolescence and melanoma^{41 56 60 68 73 76–78 81 84–86} (see table 2). In the Elwood and Jopson¹⁰ review, seven of these studies^{56 70 73–75 78 79 87} were included in a pooled analysis. The odds ratios from individual studies range from 0.7 to 2.4; the overall summary odds ratio based on these studies (age range for sun exposure approximately 12–20 years) with a total of 1826 cases was 1.73 (95% CI 1.44 to 2.07). Five of the seven studies reported an increased risk of melanoma with history of sunburn during adolescence. Summary estimates were calculated by Elwood and Jopson¹⁰ for these five studies excluding the two studies that were classified as outliers. The summary odds ratio was 1.95 (95% CI 1.60 to 2.36) based on 1723 cases. The lower bound of the majority of the confidence intervals presented for the studies (5 of 7) was at or above the null value of 1.0, indicating the possible range of the true increased risk associated with sunburn history.

Despite the strong evidence of sunburns during childhood and adolescence being a critical time period for the future development of melanoma, a handful of studies have not provided evidence of this “critical period”.^{82 83 88} In a case-control study of 413 cases and 416 controls by Bataille and colleagues,⁸² sunburns before the age of 15 years were not associated with melanoma after adjustments for age, gender, and skin. Some studies have also suggested that sun exposure during adulthood is just as influential as sun exposure during childhood and adolescence.^{83 88} Pfahlberg and colleagues,⁸⁸ in a case-control study of 603 melanoma cases and 627 population controls from 11 participating centres in seven European countries, determined that the magnitude of melanoma risk is equally significant with an increasing number of sunburns during both childhood (OR = 2.0, 95% CI 1.2 to 3.5) and adulthood (OR = 2.1, 95% CI 1.4 to 3.3).

In a study by Autier and Dore,¹¹ the joint effects of sun exposure during childhood and adulthood on melanoma risk were investigated. The findings suggest that adults who had intense childhood sun exposure are at the highest risk of melanoma (OR = 4.5, 95% CI 1.6 to 12.5, comparing high childhood and high adulthood sun exposure to low childhood and low adulthood sun exposure). However, the effects of sun exposures during childhood and adulthood were found to be not simply additive, and there was evidence to support a multiplicative interaction between sun exposures during these time periods. Therefore, high childhood sun exposure only led to significant melanoma risk if there was substantial sun exposure during adult life. This study showed that sun exposure during childhood and adulthood are interdependent in terms of melanoma risk.

In Whiteman’s review, 10 case-control studies that reported melanoma risks associated with personal sun exposure during two or more age periods found no consistent findings.^{35 36 38 56 62 74 77–79 86} Three case-control studies reported higher melanoma risk associated with childhood sun exposure,^{41 70 75} while one study reported higher risk associated with adulthood sun exposure.⁷⁷ Five case-control

What is already known on this topic

- While melanoma is thought to be rare in individuals under the age of 20 years, recent evidence has indicated a rapidly rising incidence of melanoma in children and teenagers
- Although there remains controversy about the age period when most of an individual's exposure occurs, epidemiological studies have revealed a strong association between sun exposure during critical periods of early life and subsequent risk of melanoma during adulthood

What this study adds

- A comprehensive summary of epidemiological research on sun exposure during childhood and adolescence and future melanoma risk
- Public health recommendations for skin cancer education programmes

studies reported similar melanoma risk regardless of sun exposure age.^{38 56 74 79 86}

Whiteman and Green⁸⁹ also conducted a review of the literature and calculated pooled estimates of melanoma risk associated with sunburn history. Sixteen case-control studies were initially identified for inclusion; however, only two studies had comparable definitions of sunburn to pool the results. The overall risk of melanoma in those who reported ever having a sunburn was 2.0 (95% CI 1.6 to 2.6); numerous episodes of severe sunburn were associated with a 3.7-fold increased risk of melanoma. Analyses were also done to examine the relation between childhood sunburn and risk of melanoma; however, only three studies met the inclusion criteria used by Whiteman and Green⁸⁹ for these analyses.^{36 70 75} Because the odds ratios were heterogeneous based on statistical testing, the authors did not attempt to pool the data and concluded that these studies do not support a positive relation between childhood sunburn and increased risk of melanoma. The odds ratios from these three individual studies ranged from 2.1 to 8.9.

DISCUSSION

We reviewed the literature on sun exposure during childhood and adolescence and risk of melanoma skin cancer during adulthood. Migrant studies generally indicate an increased melanoma risk in individuals who spent childhood in sunny geographical locations, and decreasing melanoma risk with older age at arrival to a sunny location. Individuals who resided in geographical locations close to the equator and close to the coast during childhood and/or adolescence have an increased melanoma risk compared to those who lived at higher latitudes and never lived near the coast during the same age period. Studies on intermittent sun exposure during vacation, recreation, or occupation are variable. To date, the majority of sunburn studies suggest a positive association between early age sunburn and subsequent risk of melanoma.

There was significant variation in the methodologies used for the assessment of sun exposure in the studies and there was potential for bias from misclassification in almost all of the studies. It is quite difficult to measure sun exposure accurately. Sun exposure has been quantified in a variety of ways, including: cumulative amount of exposure, type of exposure (e.g. recreational), pattern of exposure (chronic versus intermittent), and frequency of sunburn. Various approaches have been utilised to define and measure these exposures. Epidemiological studies commonly use questionnaires to obtain information on exposures of interest when studying large groups of people in free living populations. This approach has been widely adopted for the study of sun exposures and skin cancer, although inherently there is the potential for both differential and non-differential misclassification.^{87 90} Differential misclassification, resulting from

recall bias may have affected the results in these studies if diseased cases over- or under-reported sun exposure history compared to non-diseased controls. Furthermore, the association between sun exposure during childhood and adolescence and melanoma may be underestimated due to the random misclassification of early life exposures. This may explain the inconsistent results between studies, as well as the relatively weak observed associations.

Several studies have reported on the reliability or reproducibility of sun exposure measures.^{63 87 90-95} Most studies have shown that retrospective assessment of sun exposure in adults is not indicative of the actual amounts and patterns of exposure, nor are the results reproducible.^{63 91 92} In a few studies, however, habitual sun exposure in adolescents was identified as a stable behaviour that is reported with an acceptable degree validity and reliability,⁹³ while sun exposure in adults has been reported with high levels of validity⁹⁵ and fair to good reliability.⁹⁴

Prospective studies assessing sun exposure during different time periods of life (childhood, adolescence, young adulthood) using a reliable and quantitative method for determining ultraviolet exposure are important. Work has been done to establish standards for determining ultraviolet radiation exposure,⁹⁶ which suggests the need for further research. To understand the aetiology of skin cancer, especially melanoma, and the effect of sun exposure during different time periods of life, detailed and valid exposure information must be obtained on age at first sunburn, age at last sunburn, and number of sunburns. Information should also be obtained for protective measures, such as sunscreen use and wearing of protective clothing, to allow for adjustment in the analyses.

In studies of sun exposure and melanoma, estimates of effect will be influenced by adjustment or lack of adjustment for sun sensitivity and any related "genetic susceptibility". There is variability in individual response to ultraviolet radiation exposure which has been characterised by phenotypic measures, hair, eye, and skin colour, skin type, freckling, propensity to burn versus tan, and number of nevi. Some studies, although not all, suggest an increased risk associated with individuals who burn easily and tan poorly and are thus inherently susceptible to the effects of the sun.⁷⁴ Studies assessing the effect of sun exposure on risk of melanoma may be confounded (negatively) by lack of adjustment for sun sensitivity and there may be an interaction between exposure and susceptibility. Furthermore, pigmentary traits, eye, hair, and skin colour are highly correlated with each other as well as with the ability to tan. Controlling for skin type when studying sunburn and melanoma has the potential to obscure an association because skin type is a determinant of sunburn and highly correlated with sunburn. Studies should focus on examining the interrelations between ability to tan, propensity to burn, skin type, history of sunburns, timing and pattern of sun exposure, number of nevi, and other host factors.

As skin cancer education programmes directed to children and adolescents continue to expand, an epidemiological basis for these programmes is necessary to target efforts and plan for further evaluation. There is the possibility that negative studies susceptible to publication bias may have been

underrepresented in our review. Future research studies may help to clarify the relation between sun exposure during this time period of life and risk of melanoma during adulthood. Future research efforts should focus on: (1) clarifying the relation between sun exposure and melanoma; (2) conducting prospective studies; (3) assessing sun exposure during different time periods of life using a reliable and quantitative method; (4) obtaining information on protective measures; and (5) examining the interrelations between ability to tan, propensity to burn, skin type, history of sunburns, timing and pattern of sun exposure, number of nevi, and other host factors in the child and adolescent populations.

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