Overseas Sun Exposure, Nevus Counts, and Premature Skin Aging in Young English Women: A Population-Based Survey

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A large number of melanocytic nevi is the strongest known risk factor for melanoma in whites, but its relationship to sun exposure overseas among young white women living in temperate climates is unclear. A total of 754 white English women aged 18–46 years were recruited into a cross-sectional study in 1997–2000 to investigate the effect of ultraviolet exposures on numbers of nevi and atypical nevi, and on skin aging as measured by microtopography. Having ever holidayed in hotter countries was associated with a greater age- and phenotype-adjusted mean number of whole-body nevi (percent increase = 74; 95% confidence interval: 24, 144; $P = 0.001$), particularly for holidays taken at ages 18–29 years and for counts of the trunk and lower limbs. Having ever lived overseas was not associated with nevus counts, but was inversely associated with number of atypical nevi ($P = 0.02$). Skin aging was not associated with residence or holidays abroad. The association of holidays overseas with an increased nevus count in young white women, which was stronger in the anatomical sites intermittently exposed to sunlight, supports the hypothesis that intermittent sun exposure is of relevance in the etiology of nevi and, hence, melanoma. The findings are of public health relevance given the growing popularity of foreign holidays.

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INTRODUCTION

The increase in the incidence of malignant melanoma in white populations over many decades (Swerdlow *et al.*, 2001; Parkin *et al.*, 2005) has paralleled the increases in leisure time sun exposures, particularly ''intermittent'' exposures (Armstrong, 1988; Elwood and Jopson, 1997; Gandini *et al.*, 2005a). Basal cell carcinoma and squamous cell carcinoma have also been linked to solar radiation, but whereas cumulative lifetime exposure is the most important risk factor for squamous cell carcinoma, cumulative and intermittent exposures play a role in the etiology of basal cell carcinoma (Armstrong and Kricker, 2001).

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Abbreviation: CI, confidence interval

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A large number of benign nevi (moles) is one of the strongest known risk factors for melanoma skin cancer (Swerdlow *et al.*, 1986; Bain *et al.*, 1988; Marrett *et al.*, 1992; Bataille *et al.*, 1996; Grulich *et al.*, 1996; Gandini *et al.*, 2005b). Both nevi and melanoma arise from melanocytes, the pigment-producing cells of the skin, and therefore the association between number of nevi and melanoma risk suggests that nevi are either markers of inherited susceptibility to melanocytic proliferation and/or some environmental exposure that leads to melanoma or potential precursors of melanoma. Thus, they offer the potential to be used as an early intermediate end point to study the etiology of melanoma and evaluate the efficacy of risk-reduction interventions. Twin studies showed that although variation in nevus number is to a large extent genetically determined (Zhu *et al.*, 1999; Wachsmuth *et al.*, 2001), environmental factors are also important. Actinic skin damage has also been found to be associated with melanoma (Holman *et al.*, 1984a; Gandini *et al.*, 2005c) and non-melanoma skin cancer (Green *et al.*, 1988).

Young women, who have the highest sun exposure (Melia and Bulman, 1995; Jackson *et al.*, 1999) and desire for a sun tan (Jackson *et al.*, 1999), are unlikely to change their sun-related behavior purely on the basis of increased risk of a relatively rare tumor later in life. They may, however, be persuaded to change their behavior if sun exposure has more

immediate adverse cosmetic effects (Kligman, 1969; Green, 1991). Holidays overseas in hotter countries, with higher ambient UV levels, have increased markedly in the last decades (Swerdlow *et al.*, 2001). This paper investigates the effect of foreign sun exposure on nevus count and skin aging among young white women living in a temperate climate such as the United Kingdom.

RESULTS

Characteristics of the study population

A total of 1,408 women (63%) replied to the initial postal questionnaire and were invited for a detailed interview. Complete questionnaire and whole-body skin examination data were obtained for 754 women. Of these, 56% were recruited in Yorkshire. The characteristics of the participants are summarized Table 1. There was considerable interindividual variability in whole-body number of nevi $\geqslant 2$ mm in diameter. Only 18% of women had one or more atypical nevi.

Nevus counts on the upper limbs were correlated with the counts on the lower limbs ($r=0.71$) and, to a lesser extent, with the counts on the trunk ($r=0.62$) and head ($r=0.47$) (all $P<0.001$). Nevus counts on the lower limbs were also weakly correlated with those on the trunk ($r=0.49$) and head ($r=0.31$), and the count on the head with that on the trunk ($r=0.46$) (all $P<0.001$). Numbers of atypical nevi were only weakly correlated with the number of whole-body nevi ($r=0.25$; $P<0.001$). The distribution of face microtopography scores was negatively skewed, with 17% of women having scores above 3. A similar distribution was observed for hand scores, but their correlation with the face scores was weak ($r=0.36$; $P<0.001$).

Neither nevus counts nor the number of atypical nevi on the body were associated with age (percent change in mean number per 1 year increase in age: 0 (95% confidence interval (CI): −1, 1; $P=0.48$) for nevi and 2 (−1, 5; $P=0.30$) for atypical nevi). There was, however, a positive association between microtopography and age (percent change in mean face scores per 1 year increase in age: 3 (95% CI: 2, 3; $P<0.001$)). The mean number of whole-body nevi was highest among never-smokers and lowest among current smokers, with ex-smokers having intermediate levels (age- and interviewer-adjusted P for linear trend (P_t) $=0.06$). A similar inverse gradient with smoking habits was observed for atypical nevi ($P_t=0.04$), but not for microtopography scores ($P_t=0.9$).

The mean number of whole-body nevi was lower in women with dark brown or black hair than in those with red, blonde, or light brown hair after adjustment for interviewer, age, and smoking (ratio of mean number of nevi [RR] $=0.89$; 95% CI: 0.79, 1.00; $P=0.06$). There was no association between nevus counts and eye color. Reporting having had freckles at age 15 years was associated with a larger number of nevi (RR $=1.18$; 1.05, 1.13; $P=0.006$). Relative to women who never or hardly ever burn when exposed to midday sun without using sunscreen, the mean number of whole-body nevi was higher in those who burn sometimes and in those who burn easily or always ($P_t=0.045$). None of these phenotypic characteristics were associated with the number of atypical nevi or microtopography scores on the face or hand. Neither whole-body nevus counts nor the number of atypical nevi were associated with body mass index ($P_t=0.98$) or adult height ($P_t=0.80$). The associations of nevus counts with hair color, freckles, and skin sensitivity persisted after further adjustment for cumulative overseas residential UVB flux and the length of holidays spent abroad, but they were no longer statistically significant.

Residences abroad

Only 26% of women reported having ever lived abroad for 3 or more months in a country hotter than the United Kingdom or where most time was spent at altitude (Table 2). There were no associations between residential history abroad and the number of nevi in the whole body (Table 2) or at any specific anatomic location (data not shown). Having ever lived abroad was inversely associated with the number of atypical nevi (Table 2). Among those who had ever lived abroad, the number of atypical nevi was positively associated with age when they first lived abroad, but not with the length of residence (Table 2). The number of atypical nevi was, however, negatively associated with cumulative UVB flux (Table 2). Microtopography scores on the face (Table 2) or hand were not associated with residential history abroad. Frequency of the use of sunscreen while living abroad had no effect on nevus count, atypical nevi, or microtopography (Table 2).

Holidays abroad

Of the participants, 45% reported having spent a cumulative total of 20 or more weeks holidaying in countries hotter than the United Kingdom, or where most time was spent at altitude (Table 3). Having ever spent holidays abroad was associated with a greater number of whole-body nevi (Table 3). Among those who had ever holidayed abroad, nevus count was negatively associated with age when they first holidayed abroad (Table 3). There were no associations between foreign holidays and atypical nevi or microtopography.

The association between having ever holidayed abroad and whole-body nevus counts was present regardless of the age (that is, 0–17, 18–29, or 30–44 years) when the holidays were taken, although a positive trend in the mean number of nevi with cumulative number of weeks of holidays was observed only for holidays taken at ages 18–29 years ($P_t=0.03$) (data not shown). Associations at older ages may reflect the fact that women who holidayed abroad at these ages were likely to have holidayed abroad at younger ages, and vice versa, but mutually adjusted estimates were similar (for example, the RR for having ever holidayed abroad at ages 18–29 years was 1.38 (95% CI: 1.11, 1.72) and 1.31 (95% CI: 1.06, 1.63), respectively, before and after adjustment for having ever holidayed abroad at ages 0–17 years). The effect of foreign holidays on nevus counts was not modified by attained age.

The effect of having ever holidayed abroad on nevus counts appeared to be strongest for the lower limbs and the trunk than for the upper limbs, particularly for holidays taken

Table 1. Characteristics of the study participants, England (*N*=754 women)

	Number (%)	Mean (SD)	Median (range)
Age at interview (years)		36.2 (6.6)	37.4 (19–46)
18–29	145 (19.2)		
30–39	339 (45.0)		
40–46	270 (35.8)		
Smoking habits			
Never	445 (59.1)		
Ex-smoker	188 (25.0)		
Current smoker	120 (15.9)		
Missing	*1 (0.1)*		
No. of nevi (⩾2 mm)			
Whole body		57.6 (47.1)	45 (0–355)
0–19	148 (19.7)		
20–49	264 (35.2)		
50–79	150 (20.0)		
80–120	110 (14.7)		
120+	78 (10.4)		
Missing	*4 (0.5)*		
Head[1]		5.0 (4.8)	4 (0–44)
Trunk[2]		12.8 (12.0)	9 (0–119)
Upper limbs[3]		22.5 (19.1)	17 (0–111)
Lower limbs[4]		17.4 (20.3)	10 (0–140)
No.of atypical nevi			
Whole body		0.34 (0.89)	0 (0–7)
0	616 (82.0)		
1	70 (9.3)		
2	33 (4.4)		
3+	32 (4.3)		
Missing	*3 (0.4)*		
Head[1]		0.01 (0.07)	0 (0–1)
Trunk[2]		0.23 (0.7)	0 (0–6)
Upper limbs[3]		0.05 (0.28)	0 (0–3)
Lower limbs[4]		0.06 (0.29)	0 (0–3)
Microtopography score		2.7 (1.2)	3 (0–5)
Hand			
0	57 (7.6)		
1	54 (7.2)		
2	191 (25.4)		
3	271 (36.0)		
4	130 (17.3)		
5	50 (6.5)		
Missing	*1 (0.1)*		
Face (peri-orbital area)		2.5 (1.2)	3 (0–5)
0	69 (9.2)		
1	87 (11.6)		
2	161 (21.4)		
3	309 (41.0)		
4	112 (14.9)		
5	15 (2.0)		

[1]Includes face, scalp, and neck; data missing for one woman.
[2]Includes chest, abdomen, back, and buttocks; data missing for one woman.
[3]Data missing for two women.
[4]Includes feet; data missing for one woman.

at ages 18–29 years, with mean nevus counts in these sites increasing with increasing total weeks holidayed only at these ages (Table 4). The effect of foreign holidays was observed for both the upper and lower legs, but a positive trend in nevus counts with total weeks holidayed was observed only for the upper legs (Table 4).

The holiday abroad variable combined beach and non-beach holidays in countries hotter than the United Kingdom with holidays at altitude. Most holidays abroad were beach holidays, but the association between having ever holidayed abroad and whole-body nevus count was similar among women who had only non-beach holidays and those who had beach holidays. Beach holidays taken at ages 18–29 years were, however, more strongly associated with nevus count in the trunk ($P_t = 0.048$), whereas non-beach holidays at the same ages were more strongly associated with nevus counts in the arms ($P_t = 0.069$) and upper legs ($P_t = 0.032$). Holidays at altitude represented only 5% of all holidays, and their exclusion from the aggregated exposure measure did not affect the findings reported here.

Further adjustment for the history of sunburns, UK leisure and occupational outdoor exposures had little impact on the overseas holiday associations reported here. There was little evidence that the effect of foreign holidays on nevus counts on the trunk and lower limbs was modified by phenotype, except for borderline evidence that the effect of total length of holidays spent abroad at ages 18–29 years, but not at other ages, might be more marked in women with blonde, red, or light brown hair than in those with dark brown or black hair (Table 5).

DISCUSSION

This study found that foreign holidays in countries hotter than the United Kingdom, or where most time was spent at altitude, were positively associated with whole-body nevus counts in white young women living in England. Among those who had ever holidayed abroad, nevus count was inversely associated with age when they first holidayed abroad. The association between foreign holidays and nevus

Table 2. Whole-body nevus count and skin aging in relation to residential history abroad for more than 3 months in places hotter than the United Kingdom (or at altitude)

		No. of nevi (⩾2 mm)			No. of atypical nevi			Face microtopography score		
	N (%)	Mean (SD)	RR[1]	95% CI[2]	Mean (SD)	RR[1]	95% CI[2]	Mean (SD)	RR[1]	95% CI[2]
Ever lived abroad										
No (baseline)	555 (73.6)	58.6 (49.0)	1.00		0.4 (0.9)	1.00		2.5 (1.2)	1.00	
Yes	199 (26.4)	54.6 (41.3)	0.96	0.85, 1.09	0.3 (0.8)	0.67	0.47, 0.94	2.5 (1.2)	0.99	0.92, 1.06
P het[3]			*0.54*			*0.02*			*0.71*	
Age first lived abroad (years)										
Never (baseline)	555 (74.6)	58.6 (49.0)	1.00		0.4 (0.9)	1.00		2.5 (1.2)	1.00	
0–17	68 (9.1)	62.1 (43.3)	1.05	0.88, 1.25	0.2 (0.5)	0.46	0.28, 0.78	2.3 (1.2)	0.95	0.84, 1.08
18–29	111 (14.9)	50.9 (38.3)	0.92	0.79, 1.07	0.4 (0.9)	0.76	0.51, 1.14	2.4 (1.2)	0.98	0.89, 1.07
30–44	10 (1.3)	59.2 (51.9)	1.07	0.63, 1.83	0.6 (1.1)	1.01	0.46, 2.26	3.3 (1.4)	1.16	0.94, 1.43
Missing	10 (1.3)									
RR per 1-year increment			1.00	0.98–1.01		1.03	1.01–1.06		1.00	1.00–1.01
P-trend[4]			*0.47*			*0.02*			*0.32*	
Total length of time lived abroad (years)										
Never (baseline)	555 (74.5)	58.6 (49.0)	1.00		0.4 (0.9)	1.00		2.5 (1.2)	1.00	
<1	65 (8.7)	54.0 (42.3)	0.96	0.79, 1.17	0.3 (0.6)	0.57	0.32, 1.00	2.4 (1.3)	0.99	0.87, 1.12
1–2	59 (7.9)	56.8 (41.7)	1.02	0.84, 1.22	0.4 (1.0)	0.85	0.51, 1.42	2.3 (1.2)	0.89	0.77, 1.03
3+	66 (8.9)	55.6 (39.8)	0.95	0.79, 1.15	0.3 (0.7)	0.65	0.38, 1.13	2.6 (1.1)	1.05	0.96, 1.15
Missing	9 (1.2)									
RR per 1-year increment			1.00	0.98–1.02		0.96	0.92–1.01		1.00	0.98–1.10
P-trend[4]			*1.0*			*0.12*			*0.59*	
Cumulative UVB dose while living abroad (R–B units)										
None (baseline)	555 (74.5)	58.6 (49.0)	1.00		0.4 (0.9)	1.00		2.5 (1.2)	1.00	
250,000–849,999	48 (6.4)	53.9 (46.1)	0.96	0.75, 1.22	0.3 (0.6)	0.56	0.31, 1.01	2.4 (1.3)	0.96	0.83, 1.12
850,000–2,499,999	46 (6.2)	54.7 (36.8)	0.97	0.78, 1.20	0.2 (0.5)	0.41	0.17, 0.97	2.3 (1.2)	0.94	0.81, 1.08
2,500,000–7,499,999	50 (6.7)	52.1 (36.3)	0.93	0.76, 1.12	0.5 (1.1)	1.02	0.65, 1.59	2.5 (1.2)	1.00	0.88, 1.15
7,500,000+	46 (6.2)	61.2 (44.8)	1.05	0.84, 1.31	0.3 (0.7)	0.65	0.28, 1.49	2.5 (1.1)	1.01	0.90, 1.13
Missing	9 (1.2)									
RR per million increment			1.00	1.00–1.01		0.98	0.97, 1.00		1.00	0.99–1.00
P-trend[4]			*0.63*			*0.05*			*0.10*	
Use of sunscreen while abroad										
Never abroad	555 (75.7)	58.6 (49.0)	1.00		0.4 (0.9)	1.00		2.5 (1.2)	1.00	
Abroad, but never use	82 (11.2)	54.9 (44.9)	0.96	0.80, 1.16	0.4 (0.8)	0.73	0.46, 1.16	2.4 (1.2)	0.93	0.83, 1.04
Abroad, fairly often use	53 (7.2)	57.0 (38.1)	1.03	0.85, 1.25	0.3 (0.7)	0.61	0.33, 1.14	2.4 (1.2)	1.00	0.88, 1.13
Abroad, always use	43 (5.9)	56.2 (39.6)	0.98	0.79, 1.22	0.3 (0.8)	0.89	0.46, 1.71	2.6 (1.2)	1.02	0.90, 1.17
Missing	21 (2.8)									
P-trend[4]			*0.88*			*0.42*			*0.16*	

R–B, Robertson–Bergen.
England (*N*=754 women).
[1]Ratio of the mean number of nevi in each category of the explanatory variable relative to the baseline category, adjusted for interviewer, age at interview, smoking status, and the phenotypic characteristics shown in table.
[2]95% confidence interval.
[3]*P*-value for heterogeneity.
[4]*P*-value for linear trend among those exposed and, for quantitative variables, in their original continuous scale.

Table 3. Whole-body navus count and skin aging in relation to holidays spent abroad in countries hotter than the United Kingdom (or at altitude)

		No. of nevi (⩾2 mm)			No. of atypical nevi			Face microtopography score		
Holidays abroad	***N*** **(%)**	**Mean (SD)**	**RR[1]**	**95% CI[2]**	**Mean (SD)**	**RR[1]**	**95% CI[2]**	**Mean (SD)**	**RR[1]**	**95% CI[2]**
Ever holidayed										
No	26 (3.5)	36.2 (32.6)	1.00		0.2 (0.8)	1.00		2.5 (1.3)	1.00	
Yes	725 (96.2)	58.5 (47.4)	1.74	1.24, 2.44	0.3 (0.9)	1.24	0.36, 4.37	2.5 (1.2)	0.92	0.78, 1.07
Missing	3									
P het[3]			*0.001*			*0.73*			*0.27*	
Age first holidayed abroad (years)										
Never	26 (3.5)	36.2 (32.6)	1.00		0.2 (0.8)	1.00		2.5 (1.3)	1.00	
0–17	424 (56.2)	62.9 (48.7)	1.85	1.32, 2.58	0.4 (0.9)	1.30	0.37, 4.60	2.4 (1.2)	0.91	0.78, 1.07
18–29	278 (36.9)	52.9 (45.5)	1.57	1.11, 2.22	0.3 (0.8)	1.07	0.27, 4.27	2.6 (1.2)	0.92	0.78, 1.08
30–44	26 (3.5)	42.8 (33.6)	1.25	0.80, 1.94	0.4 (1.1)	1.38	0.31, 6.14	3.0 (1.0)	0.97	0.78, 1.20
Missing	0									
RR per 1-year increment			0.85	0.76, 0.94		0.88	0.63, 1.24		1.02	0.97, 1.09
P-trend[4]			*0.003*			*0.47*			*0.42*	
Total weeks holidayed										
Never	34 (4.5)	40.9 (33.4)	1.00		0.5 (1.5)	1.00		2.3 (1.3)	1.00	
<10	171 (22.7)	53.9 (40.9)	1.33	0.98, 1.80	0.3 (0.7)	0.62	0.28, 1.37	2.3 (1.2)	1.01	0.85, 1.19
10–20	210 (27.9)	59.5 (47.6)	1.54	1.14, 2.08	0.3 (0.8)	0.55	0.25, 1.24	2.4 (1.1)	0.97	0.82, 1.15
20–34	188 (25.0)	61.9 (50.3)	1.63	1.20, 2.21	0.4 (0.9)	0.62	0.28, 1.37	2.6 (1.2)	0.98	0.82, 1.16
35+	148 (19.7)	58.5 (50.8)	1.58	1.14, 2.18	0.4 (0.9)	0.77	0.32, 1.89	2.6 (1.3)	0.95	0.80, 1.14
Missing	3									
RR per 1-week increment			1.00	1.00, 1.01		1.01	1.00, 1.01		1.00	1.00, 1.00
P-trend[4]			*0.10*			*0.11*			*0.71*	

England (*N*=754 women).
[1]Ratio of the mean number of nevi in each category of the explanatory variable relative to the baseline category, adjusted for interviewer, age at interview, smoking status, and the phenotypic characteristics shown in Table 2.
[2]95% confidence interval.
[3]*P*-value for heterogeneity.
[4]*P*-value for linear trend among those exposed and, for quantitative variables, in their original continuous scale.

count was particularly stronger for the lower limbs and the trunk, sites that are intermittently exposed to sunlight. In white women, melanomas occur most frequently on the lower limbs. The positive association of nevus count with foreign holidays, but not residences, also supports the hypothesis that intermittent exposures are etiologically more relevant than cumulative exposures. Nevus numbers have been found to be positively associated with holiday sun exposure in adolescent twins (Wachsmuth *et al.*, 2005), foreign holidays and residences in Scots (Mackie *et al.*, 1985), and holidays to hotter countries in children in Germany (Dulon *et al.*, 2002). Other studies have found residential UVB flux exposure in North America (Fears *et al.*, 2002) and annual hours of bright sunshine in Australia (Armstrong *et al.*, 1986), as markers of cumulative exposure, to be strong risk factors for melanoma. A meta-analysis of data from 40 studies supports the view that intermittent sun exposure (for example, sunbathing, sunny holidays) is etiologically the most important for melanoma (Gandini *et al.*, 2005a).

Numbers of atypical nevi were not affected by foreign holidays but were negatively associated with having ever lived abroad and with cumulative UVB dose while living abroad. Foreign residences are likely to be a marker of chronic sun exposure, and hence the findings would be consistent with the hypothesis that chronic sun exposure might be protective for atypical nevi and with the observation that atypical nevi are more frequent on normally covered body sites such as the trunk. The meta-analysis described above found that high continuous sun exposure is negatively associated with melanoma risk (Gandini *et al.*, 2005a). But

Table 4. Selected anatomical site-specific nevus counts in relation to holidays spent in countries hotter than the United Kingdom (or at altitude) at ages 18–29 years

		Trunk (chest, abdomen, back, and buttocks)			Upper limbs			Lower limbs (including feet)								
								Whole			Upper legs			Lower legs		
Holidays abroad	*N* (%)	Mean (SD)	RR[1]	95% CI[2]	Mean (SD)	RR[1]	95% CI[2]	Mean (SD)	RR[1]	95% CI[2]	Mean (SD)	RR[1]	95% CI[2]	Mean (SD)	RR[1]	95% CI[2]
Ever holidayed																
No	68 (9.0)	9.6 (9.2)	1.00		19.5 (17.6)	1.00		11.3 (15.0)	1.00		6.1 (8.5)	1.00		5.0 (6.8)	1.00	
Yes	684 (91.0)	13.1 (12.2)	1.36	1.07, 1.74	22.8 (19.2)	1.20	0.96, 1.50	17.3 (20.1)	1.73	1.27, 2.35	9.8 (12.2)	1.80	1.31–2.48	7.3 (8.9)	1.67	(1.21–2.29)
Missing	2 (0.3)															
P het[3]			*0.01*			*0.10*			*<0.001*			*<0.001*			*0.002*	
Total weeks holidayed																
Never	68 (9.0)	9.6 (9.2)	1.00		19.5 (17.6)	1.00		11.3 (15.0)	1.00		6.1 (8.5)	1.00		5.0 (6.8)	1.00	
<4	68 (9.0)	11.0 (10.7)	1.13	0.82, 1.57	22.2 (15.3)	1.14	0.87, 1.49	14.4 (14.6)	1.45	0.98, 2.16	7.8 (8.7)	1.43	0.93, 2.19	6.5 (7.1)	1.48	0.99, 2.22
4–9	201 (26.7)	11.6 (10.7)	1.20	0.92, 1.56	21.4 (18.0)	1.08	0.85, 1.37	15.3 (17.8)	1.42	1.02, 1.98	8.6 (11.6)	1.44	1.01, 2.05	6.6 (7.3)	1.42	1.01, 1.99
10–19	227 (30.2)	13.7 (13.2)	1.44	1.10, 1.89	23.7 (21.1)	1.27	1.00, 1.62	20.4 (22.9)	2.02	1.46, 2.80	11.9 (13.7)	2.17	1.55, 3.05	8.4 (10.1)	1.88	1.33, 2.64
20+	188 (25.0)	14.8 (12.6)	1.55	1.19, 2.02	23.3 (19.5)	1.28	1.00, 1.64	16.8 (20.0)	1.79	1.28, 2.50	9.4 (11.6)	1.88	1.33, 2.66	7.2 (9.5)	1.72	1.21, 2.46
Missing	2 (0.3)															
RR per 1-week increment			1.01	1.00, 1.02		1.01	1.00, 1.01		1.01	1.00, 1.01		1.01	1.00, 1.02		1.00	1.00, 1.01
P-trend[4]			*0.008*			*0.09*			*0.06*			*0.03*			*0.22*	

England (*N*=754).
[1]Ratio (95% CI) of the mean number of nevi in each category of the explanatory variable relative to the baseline category, adjusted for interviewer, age at interview, smoking habits, and phenotypic characteristics.
[2]95% confidence interval.
[3]*P*-value for heterogeneity across exposure categories.
[4]*P*-value for linear trend among those who had ever holidayed abroad, in its original continuous scale.

these negative associations with continuous exposures might simply reflect residual confounding by intermittent exposures, as the two types of sun exposure tend to be negatively correlated.

Microtopography scores were positively associated with age, consistent with cumulative sun exposure being a risk factor for skin aging. There was, however, no association between history of residence or holidays abroad and microtopography. In Australia, where UV flux is far greater than the United Kingdom, high scores are strongly associated with correlates of cumulative sun exposure, such as solar keratoses (Holman *et al.*, 1984a; Green, 1991), nonmelanoma skin cancer (Holman *et al.*, 1984a; Green, 1991; Kricker *et al.*, 1991), and increasing age (Beagley and Gibson, 1980; Green, 1991).

Strengths and weaknesses

This study was a population-based survey of young white women living in England with detailed data on a large number of UV exposure variables and a whole-body skin examination. The response rate to the initial postal survey (63%) can be regarded as good and similar to those of other surveys of young women. Responders might have differed from non-responders in relation to the exposures and outcomes of interest if, for instance, those with heavy sun exposures and sun-damaged skin were more or less inclined to participate than those with heavy sun exposures but little skin damage. This is unlikely, however. Only 54% of those invited for the detailed interview completed it, but there were no major demographic or sun-related behavioral differences, as assessed by the postal questionnaire, between those who completed the interview and those who did not. Unexpectedly, whole-body nevus counts and the number of atypical nevi were higher among never-smokers than smokers. Although smoking habits might be a marker of socioeconomic status, smoking was not associated with having ever holidayed or lived abroad. However, the extent to which the study findings are generalizable to women living in other temperate climate countries is unclear.

It is notoriously difficult to recall accurately past sun exposures. Moreover, the radiation dose actually received is greatly modified by the immediate environment, nature of the activity being undertaken, type of clothing, sunscreen use, and other factors. In this study, exposure misclassification would most likely have been non-differential, therefore biasing the sun exposure effect estimates toward the null. This might explain why we found no positive trends in nevus counts with length of foreign holidays at ages 0–17 years, as

Table 5. Nevus counts on the trunk and lower limbs in relation to foreign holidays at ages 18–29 years, by selected phenotypic characteristics

	Having ever holidayed overseas			Per 1-week increment in holidays overseas		
Phenotypic variable anatomic site	**RR[1]**	**95% CI[2]**	***P*-value for interaction**	**RR[3]**	**95% CI[2]**	***P*-value for interaction**
Hair color						
Trunk						
Blonde/red/light brown	1.34	0.99, 1.82	*0.73*	1.02	1.01, 1.02	*0.05*
Dark brown/black	1.34	0.92, 1.95		1.00	0.99, 1.01	
Lower limbs						
Blonde/red/light brown	1.48	1.00, 2.18	*0.15*	1.01	1.00, 1.02	*0.04*
Dark brown/black	2.32	1.51, 3.57		1.00	0.99, 1.01	
Freckles at age 15						
Trunk						
No	1.46	0.92, 2.31	*1.00*	1.02	1.01, 1.03	*0.12*
Yes	1.34	1.01, 1.76		1.01	1.00, 1.01	
Lower limbs						
No	1.83	1.04, 3.20	*0.92*	1.01	1.00, 1.03	*0.29*
Yes	1.69	1.18, 2.40		1.00	1.00, 1.01	
Skin sensitivity to midday sun						
Trunk						
Never/hardly ever/sometimes burns, tans easily	1.40	1.06, 1.84	*0.65*	1.01	1.00, 1.02	*0.31*
Burns easily/always, never tans or tans eventually with difficulty	1.16	0.70, 1.94		1.01	1.00, 1.02	
Lower limbs						
Never/hardly ever/sometimes burns, tans easily	1.81	1.28, 2.56	*0.51*	1.00	1.00, 1.01	*0.68*
Burns easily/always, never tans or tans eventually with difficulty	1.40	0.77, 2.54		1.01	1.00, 1.02	

England (*N*=754 women).
[1]Ratio of the mean number of nevi (⩾2 mm) in women who had ever holidayed overseas at ages 18–29 relative to the mean number in those who had never been on foreign holidays at ages 18–29 years.
[2]95% confidence interval.
[3]Relative ratio in mean number of nevi (⩾2 mm) per 1 week increase in total length of holidays spent overseas at ages 18–29 years.

women may have found it particularly difficult to recall accurately the length of their foreign holidays in childhood. It is, however, unlikely that recall would be biased by nevus count, as subjects were unaware of their counts or of the hypothesized relation to foreign sun exposure. No information was collected on which parts of the body were exposed to the sun, but the differential effects on site-specific nevus counts of beach and non-beach holidays are consistent with beach versus non-beach differences in exposure of different parts of the body to the sun.

The measure of foreign residence UVB exposure used here, while incorporating latitude and duration, was nevertheless imprecise. Data on exact place of residence were not available, making estimation of latitude inexact and estimation of altitude, cloud cover, and ozone levels impossible. Whereas 97% of variation in UVB levels across the United States is explained by latitude, altitude, and sky cover, only 68% is explained by latitude alone (Scotto *et al.*, 1996).

The analyses were adjusted for interviewer to minimize the effect of inter-observer variation. Because of the cross-sectional nature of the study, the nevus counts are prevalent counts and the reported RRs should be interpreted as prevalent rather than incident measures of exposure effect. Most visible nevi are acquired after birth, particularly around

puberty, declining first in incidence and then in number after young adulthood (Mackie *et al.*, 1985; Green and Swerdlow, 1989), but the potential confounding effect of age was dealt with in the analysis. Sunlight promotes both nevus development and disappearance (Green and Swerdlow, 1989). This dual effect would attenuate any association between sun exposure and nevus counts measured at a single point in time, but its impact would have been small given the relatively young study population.

Microtopography has been widely used (Beagley and Gibson, 1980; Holman *et al.*, 1984a; Green, 1991; Kricker *et al.*, 1991) and validated as a measure of skin damage in heavily sun-exposed populations (Holman *et al.*, 1984a). We adapted this method to the lower UK sunlight levels. The value of this modified approach as a correlate of actinic skin damage, or as a predictor of cancer, has not been assessed but its scores were strongly correlated with age, a marker of cumulative UV exposure. The lack of correlation between microtopography and foreign sun exposure suggests that skin aging in young women living in a temperate climate is determined by other factors, or that the method used was too insensitive.

Subjects with a tendency to burn rather than tan, and hence an increased *a priori* risk of harmful UV effects, may avoid high-exposure activities. Thus, the presence of unfavorable phenotypic characteristics may have exerted negative confounding on the association of foreign sun exposures with nevus counts and microtopography. Although our analyses adjusted for phenotype and UK sun-related exposures, the measurements of these variables were inevitably imprecise, and hence residual confounding could still have occurred, as the various types of UV exposures and phenotype tend to be correlated. Finally, some statistically significant results may have arisen by chance given the large number of statistical tests performed. Conversely, the power of our statistical models to detect interactions was limited. As the number of women with atypical nevi was small the power in relation to this endpoint was particularly low.

Conclusions

This study assessed the effect of foreign sun exposures in young white women living in a temperate climate. To our knowledge this is previously unreported. Holidays in hotter countries were associated with increased nevus counts, particularly in the trunk and lower limbs, which are exposed to sunlight only intermittently. This study supports the hypothesis that intermittent sun exposures are the main environmental risk factor for nevus counts and, hence, for melanoma in temperate climates. These findings are of public health relevance given the growing popularity of foreign holidays.

MATERIALS AND METHODS

Study population

A population-based sample of women resident in Hertfordshire (St Albans) and Yorkshire (Leeds and Harrogate), England, was identified from age–sex registers from three general practices. These were selected, partly, to reflect a north–south gradient in UV exposure in England and partly for logistic reasons. All white women aged 18–46 years who were registered in these practices in 1997–2000 were sent a brief postal questionnaire. Respondents who reported that they had not suffered from any chronic skin condition were invited for an interview and whole-body skin examination conducted by one of three nurses at their general practice or, if the women preferred, at home. The study complied with the Declaration of Helsinki Principles and was approved by relevant ethics committees. Written consent was obtained from all participants.

Exposure measurements

The interviewer-administered questionnaire collected detailed information on UV-related exposures, including residential and holiday histories in the United Kingdom and overseas, outdoor leisure and occupational activities, sunbathing and sunbed use. Residences abroad were defined as those for a period of at least 3 months in a country hotter than the United Kingdom or where most time was spent at altitude. Length of holidays abroad was estimated by combining data on beach and non-beach holidays to countries hotter than the United Kingdom with data on holidays spent at high altitude (for example, skiing). Information was collected on natural skin reaction when exposed to midday sun without sunscreen (graded according to a modified Fitzpatrick (1988) score, which accounts for the skin's propensity to burn and tan), and freckling and natural hair color at the age of 15 years.

Each place of residence abroad was assigned a latitude (National Imagery and Mapping Agency, 2006). If only country of residence was indicated, latitude was assumed to be that of the capital city. Where only a region was specified, the midlatitude between the most northerly and the most southerly capital cities in that region (Interparliamentary Union, 2006) was taken. A regression equation, derived from 11 years of ground-level measurements at over 30 US stations (Scotto *et al.*, 1996), was used to estimate annual amount of UVB, in Robertson–Bergen (R–B) units, reaching the earth's surface at each place of residence overseas: $\mathrm{Ln}(\mathrm{UVB}) = 15.545 - 0.039(L) + 0.0001038(A)$, where L represents latitude (degrees north) and A altitude (in meters). A count of about 440 R–B units is equivalent to 1 minimal eritemal dose (MED) for an ''average'' Caucasian skin (Scotto *et al.*, 1996). As the exact location of residence was unknown, altitude was set at sea level. An individual's cumulative UVB flux received at all residential locations abroad (U) was calculated as $U = \Sigma u_i d_i$, where u_i indicates the average annual UVB flux in the ith residential location abroad and d_i the duration (years) of residence in the ith location. Similar approaches to combine sun exposure at different locations were used in previous studies (Holman and Armstrong, 1984; Fears *et al.*, 2002).

Outcome measurements

The three nurses were trained by the same dermatologist (JAN-B) to conduct whole-body skin examinations (except for breast and genitalia), including separate counts of nevi $\geqslant 2$ mm in diameter and atypical nevi (that is, $\geqslant 5$ mm in diameter, with an irregular or blurred edge and irregular pigmentation), by anatomical location—the head (face, scalp, and neck), trunk (chest, abdomen, back, and buttocks), upper limbs, and lower limbs (including feet). Observer variability was monitored at 6-month intervals, with each nurse independently counting nevi in the same five patients and reviewing their counts together with the dermatologist.

Skin aging was assessed by microtopography of the dorsal surface of the right hand and of the lateral peri-orbital area of the right eye, two sites consistently exposed throughout life to UV radiation, by using a fast-setting liquid impression material (Silflo, Bayer, Germany). We attempted to classify the Silflo casts according to the six-category classification developed by Beagley and Gibson (1980) for the Australian population (Holman *et al*., 1984a, b; Green, 1991). This classification provided poor discrimination because, by Australian standards, the UK casts were relatively undamaged. Instead, they were visually ranked according to texture degradation based on the depth of wrinkles from 0 (no damage) to 5 (severe damage) by the dermatologist, blind to the questionnaire and skin examination data.

Statistical methods

Owing to overdispersion of a Poisson model and the large number of subjects with zero nevi, it was necessary to fit a zero-inflated (Cheung, 2002) negative binomial (Glynn and Buring, 1996) model to the nevus counts. Exponentiation of the coefficients of this model provided an estimate of the ratio (RR) of the mean number of nevi in any given category of an explanatory variable relative to the mean number in the baseline category. A Poisson model with zero inflation was used to model microtopography scores because there was no evidence of overdispersion. Exposure variables were categorized to obtain approximately equal numbers of subjects in each category. All analyses were adjusted for interviewer, age at interview, and smoking habits. Analyses of the effect of sun exposure on nevus counts and microtopography were further adjusted for phenotypic characteristics. Likelihood ratio and Wald tests were used to examine heterogeneity and linear trend, respectively, in the outcome variables across exposure levels (Clayton and Hills, 1993). Tests for linear trend were performed only among those exposed and, for quantitative variables, in their original continuous scale. Analyses were conducted in STATA 9.0 (Stata Corporation, 2003).

CONFLICT OF INTEREST

The authors state no conflict of interest.

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