Age-dependent interaction between sex and geographic ultraviolet index in melanoma risk

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Background: Ultraviolet (UV) exposure may not affect melanoma development equally in different sexes and ages. Whether and how these factors interact with each other in relation to melanoma risk is unknown.

Objective: This study attempts to estimate interactions among UV index (UVI), sex, and age in melanoma risk.

Methods: Melanoma incidence data were collected from 42 cancer registries. Geographic UVI was collected from local satellite stations. Negative binomial regression models were used to estimate the impact of each risk factor and their interactions.

Results: Sex, UVI, and age, as well as interactions between any 2 of these factors, were significantly associated with melanoma risk. In younger age groups, female sex is an independent risk factor for melanoma that is not affected by ambient UV exposure. In older age groups, however, female sex interacts with UV exposure as a risk factor, exhibiting a protective effect. The switching age category is 45 to 49, which correlates with dramatic hormonal changes.

Limitations: The interaction between sex and UVI is measured at an ecologic level.

Conclusions: The interaction between sex and UVI is age dependent. Female sex is an independent risk factor for early-onset melanoma, but female sex also protects against UV-associated melanoma in older age groups. (J Am Acad Dermatol 2020;82:1102-8.)

Key words: epidemiology; latitude; melanoma; sex; UV; UVI.

Melanoma is the number 1 cause of death in skin cancer[1,2] and is one of the most commonly diagnosed cancers in adolescence and young adulthood, especially in young women during their reproductive years.[3] Although most other cancer types have shown a decreasing trend of incidence rates over the past 24 years, melanoma remains one of the common cancer types with increasing trend,[4] and the epidemiologic reasons are mostly related to ultraviolet radiation (UVR), including solar UVR and indoor tanning bed use.[5,6]

The risks for melanoma in adolescence and young adulthood include white race, female sex, and environmental UVR.[7] Melanoma incidence rates increase with age for both sexes but with different patterns[8,9]: young women (<45 years) have higher incidence rates than young men, but the trend reverses at an older age—older women have lower incidence rates than older men.[9] It has been known

Abbreviations used:

UV: ultraviolet
UVI: ultraviolet index
UVR: ultraviolet radiation

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for more 30 years that melanoma incidence and mortality are higher in women than in men at younger ages.[10] Most epidemiologic studies have attributed this to lifestyle and tanning bed use by younger women[11,12] (ie, younger women are less covered under the sun and use tanning beds more often[11,12]; hence, they are more exposed to UVR). However, it was reported in a meta-analysis that in Europe tanning bed use accounted for only 5.4% of all melanoma cases.[13] Therefore, the question remains as to whether UVR can fully account for the sex difference observed in melanoma in adolescence and young adulthood, or alternatively, whether melanomas from all ages are equally affected by UVR.

CAPSULE SUMMARY

- UV exposure may differentially impact risk of melanoma by sex and age.
- The female sex plays a significant and independent role in early onset melanoma.
- More effective preventive strategies can be developed based on the understanding of sex- and age-specific melanoma causes.

Our previous studies strongly suggested negative answers to the aforementioned questions. We first described a unique change in female-to-male rate ratio during the course of aging in melanoma that showed a peak difference at reproductive age.[9] Nonmelanoma skin cancer, which is also caused by UVR exposure, did not exhibit such an age-dependent rate ratio difference between the sexes. More importantly, this rate ratio difference was observed in all ethnicities, including African Americans, whose skin is well protected from UVR. Further regression analysis of sex-specific age-standardized rates and daily average geographic ultraviolet index (UVI) revealed that melanoma incidence rates in men showed a significant association with geographic UVI, but there was no such association in women.[14] These findings are very intriguing; they strongly suggest an independent role of sex, which has always been linked to differential UVR behavior between sexes. In this study we set out to examine whether we can separate the role between UVR, age, and sex and explore potential interactions among these factors in melanoma risk.

MATERIALS AND METHODS

Registry selection and melanoma classification

For melanoma cases, tumor classification was based on the standard of the International Classification of Diseases for Oncology, Third Edition, with code C43. To obtain a relatively homogeneous ethnic background, registries from northern Europe, the United States, and Australia were selected on the basis of ethnic information. For northern Europe, countries with at least 50% of their population having a light eye color were selected.[15] This excludes most of southern European countries even though their populations are largely white. Belgium was excluded because data were not available for a 10-year period. For the United States, race information is available, so only white race was included in all selected registries. For Australia, it is known that the Northern Territory contains a large indigenous population; therefore, the Northern Territory was excluded. For all registries, the most recent 10 years of incidence rates (case and population numbers in each 5-year age category) were collected depending on data availability (Table I), either from 1998 to 2007 or from 2000 to 2009. For European countries, data were obtained from Eureg part of the International Agency for Research of Cancer website (http://eco.iarc.fr/eureg/Default.aspx). For the United States, data were downloaded from the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute via SEER*Stat software. For Australia registries, data were obtained from the International Agency for Research on Cancer publication *CI5: Cancer Incidence in Five Continents*, volume C15*plus*.

Geographic UVI data and local latitude

The local UVIs were collected as described in our previous publication.[14] Briefly, UVIs were calculated from data collected by local satellite stations. The scale of the UVI is proportional to the intensity of erythema-causing UVR doses on the Earth's surface any day at noon.[16] Daily UVIs were collected from July 1, 2002, the earliest time when the data were available, to June 30, 2014, when data were first collected for this study. Average daily UVI for this period was used for analysis. The latitude value was that of roughly the central latitude of the registry area. More details are described in the Supplemental Methods (available at http://www.jaad.org).

Statistical methods

A negative binomial regression model was used to estimate association of age, sex, and UVI with melanoma risk because although the count data (case numbers) fit a Poisson distribution, the data were overdispersed ($P < .0001$). In our model assessment,

Table I. Cancer registries, years, rates, and local UVI and latitude

Country	Registry	Years	asr-M	asr-F	UVI	Latitude
Australia	Queensland	1998-2007	60.7	43.9	9.4	20.9
	New South Wales	1998-2007	44.6	30.2	7.2	33.9
	Tasman	1998-2007	37.5	34.9	5.6	41.4
	Victoria	1998-2007	32.9	26.5	6.3	37.5
	South Australia	1998-2007	32.6	26.5	7.0	30.0
	West Australia	1998-2007	49.3	33.8	7.7	27.7
Austria	Austria	2000-2009	11.0	9.7	4.1	47.5
Czech	Czech	1998-2007	12.4	10.8	3.5	49.8
Denmark	Denmark	1998-2007	14.5	17.9	3.0	56.3
Estonia	Estonia	1998-2007	6.2	7.9	2.3	58.6
Finland	Finland	1998-2007	11.0	9.1	1.8	61.9
France	Manche/Haut-Rhin	2000-2009	12.8	13.8	3.8	47.9
Iceland	Iceland	1998-2007	11.4	20.2	1.9	65.0
Ireland	Ireland	2000-2009	11.0	14.0	3.0	53.4
Netherland	Netherland	1998-2007	13.1	16.8	3.2	52.1
Norway	Norway	1998-2007	16.6	17.5	1.9	60.5
Sweden	Sweden	2000-2009	15.5	15.9	2.2	60.1
Switzerland	Zurich	2000-2009	21.0	18.9	4.1	47.4
Germany	Brandenburg	2000-2009	8.2	7.9	3.1	52.0
	Mecklenburg	2000-2009	8.1	8.3	2.8	53.6
	Schleswig-Holstein	2000-2009	14.3	16.4	2.8	54.2
	Thuringen	2000-2009	9.8	9.6	3.5	51.0
United Kingdom	East England	2000-2009	10.1	11.0	3.0	52.2
	NW England	2000-2009	8.7	11.4	2.2	52.4
	Northern Ireland	1998-2007	9.1	12.0	3.0	54.8
	Scotland	1998-2007	10.8	12.9	2.6	56.5
	Wales	1998-2007	9.8	10.8	3.0	52.1
United States	Atlanta	2000-2009	37.7	26.3	6.7	33.7
	Greater Georgia	2000-2009	24.5	17.2	6.7	32.2
	Connecticut	2000-2009	22.9	17.3	4.9	41.6
	Detroit	2000-2009	19.7	16.4	4.9	42.3
	Hawaii	2000-2009	61.2	39.3	10.5	19.9
	Iowa	2000-2009	18.3	15.8	4.9	41.9
	Kentucky	2000-2009	22.1	16.3	5.7	37.8
	Los Angeles	2000-2009	18.4	10.8	6.9	34.1
	Louisiana	2000-2009	17.4	11.4	8.9	31.0
	New Mexico	2000-2009	18.6	11.9	6.7	34.5
	New Jersey	2000-2009	23.5	16.9	5.6	40.1
	San Francisco	2000-2009	26.8	18.2	5.7	37.8
	San Jose	2000-2009	23.3	16.3	5.7	37.8
	Seattle	2000-2009	27.5	23.6	4.3	47.6
	Utah	2000-2009	29.5	19.4	6.1	39.3

asr-F, Age-standardized rate for females; *asr-M*, age-standardized rate for males; *UVI*, ultraviolet index.

the Pearson chi-square values and degrees of freedom were used to estimate whether the data were over-dispersed when modeled with a negative binomial distribution. The time period was the same for all registries (10 years), but population size varied; therefore, log-transformed population was used as an offset. A natural log link was used for a log linear model. Comparison between models was made via log likelihood ratios and chi-square statistics.

RESULTS

All 3 factors and interactions between each 2 contribute significantly to melanoma risk

Table I lists the registries and countries, years of data collection, age-standardized sex-specific melanoma incidence rates, geographic UVIs, and latitudes. As described in the Supplemental Methods, negative binomial regression was used to assess melanoma risk. In the base model (model 1) which

Table II. Parameter estimate from different models using UVI

Model	Variable	Coefficient	Standard error	Wald 95% confidence intervals		Wald chi-Square	Pr > ChiSq	*P* value for model comparison
Model 1	Intercept	−12.312	0.0754	−12.4597	−12.164	26640.5	<.0001	
	UVI	0.1673	0.0107	0.1463	0.1883	244.47	<.0001	
	Sex	−0.1383	0.0475	−0.2314	−0.0452	8.48	.0036	
	Age	0.0631	0.0012	0.0607	0.0654	2724.68	<.0001	
	LL	−8854.7						NA
Model 2	Intercept	−12.1	0.0909	−12.2779	−11.922	17730.3	<.0001	
	UVI	0.1222	0.0148	0.0931	0.1513	67.79	<.0001	
	Sex	−0.558	0.1103	−0.7741	−0.3418	25.59	<.0001	
	Age	0.063	0.0012	0.0606	0.0653	2753.02	<.0001	
	Uvi*sex	0.0892	0.0212	0.0477	0.1308	17.74	<.0001	
	LL	−8844.1						<.0001
Model 3	Intercept	−11.945	0.1384	−12.2165	−11.674	7448.36	<.0001	
	UVI	0.0898	0.0265	0.0377	0.1418	11.43	.0007	
	Sex	−0.1398	0.0473	−0.2325	−0.0472	8.76	.0031	
	Age	0.0549	0.0028	0.0494	0.0605	378.59	<.0001	
	Uvi*age	0.0017	0.0005	0.0007	0.0028	9.98	.0016	
	LL	−8848.7						.0005
Model 4	Intercept	−11.761	0.0926	−11.9425	−11.58	16127.2	<.0001	
	UVI	0.1662	0.0103	0.146	0.1863	261.08	<.0001	
	Sex	−1.1858	0.1131	−1.4076	−0.9641	109.84	<.0001	
	Age	0.0504	0.0016	0.0472	0.0537	937.02	<.0001	
	Age*sex	0.0232	0.0023	0.0187	0.0277	103	<.0001	
	LL	−8795.6						<.0001
Model 5	Intercept	−11.313	0.1522	−11.6114	−11.015	5528.3	<.0001	
	UVI	0.0689	0.0275	0.015	0.1227	6.29	.0122	
	Sex	−1.5477	0.1481	−1.8381	−1.2574	109.15	<.0001	
	Age	0.0447	0.0029	0.0389	0.0504	231.08	<.0001	
	Uvi*sex	0.0808	0.0204	0.0409	0.1207	15.76	<.0001	
	Uvi*age	0.0013	0.0005	0.0002	0.0023	5.78	.0163	
	Age*sex	0.0228	0.0023	0.0183	0.0272	100.78	<.0001	
	LL	−8782.7						<.0001

ChiSq, Chi-square; *LL*, log likelihood; *NA*, not available; *Pr*, Pearson; *UVI*, ultraviolet index.

includes 3 factors only, all 3 variables (age, sex, and UVI) were significant contributors to melanoma risk (Table II). By sequentially adding an interaction between UVI*sex, UVI*age, or age*sex to the base model, we generated models 2, 3, and 4. Each interaction significantly improved the prediction of melanoma risk as judged by the significant *P* values for either the interaction or the model comparison or both (Table II). Model 5 included all 3 possible 2 × 2 interactions, and again it is a significantly better model than model 4. When latitude was used instead of UVI, the results were similar (Supplemental Table I; available at http://www.jaad.org); all 3 variables and their interactions showed significant contributions to melanoma risk. Note that in all models, sex exhibited a negative coefficient, revealing that overall, females showed a protective effect against melanoma risk, as the regression models used male sex as a baseline.

Female sex is an independent risk factor for melanoma diagnosed at younger age

The interaction between UVI and sex was not well documented. We next examined UVI*sex interaction by using the same negative binomial model for each age category. As shown in Table III, both models suggested that UVI was significantly associated with melanoma risk across all age categories, except for the very young age (agecat 1). Sex association with melanoma risk was age dependent in both models, with different patterns. At a very young age (0-14 years) the role of sex was uncertain, as the *P* values ranged from nonsignificant to significant in model A for various age groups (Table III). Adding UVI*sex interaction did not improve the model, meaning that sex at these age groups did not modify UVI effect.

The age 15 to 19 group was a unique group in which sex was significantly associated with

Table III. UVI, sex, and UVI-sex interaction in different age strata

	Age category/age	Model A (UVI, sex)			Model B (UVI, sex, UVI*sex)				Model comparison	
Agecat	age	LL	*P*_uvi	*P*_sex	LL	*P*_uvi	*P*_sex	*P*_uvi*sex	LLR	*P*_model
1	0-4	−91.25	.1418	.19	−91.25	.281	.606	.9997	.000	1.0000
2	5-9	−122.19	.0075	.0099	−121.49	.0048	.9529	.2477	1.391	.2380
3	10-14	−187.39	<.0001	.2065	−187.24	.0042	.3325	.6093	.302	.5820
4*	15-19	−328.50	<.0001	**.0019**	−325.82	.0055	**.001**	**.0304**	5.374	**.0204**
5	20-24	−389.39	<.0001	**<.0001**	−387.88	.0008	**<.0001**	.0941	3.013	.0826
6	25-29	−441.87	<.0001	**<.0001**	−440.45	.0055	**.001**	.1074	2.848	.0915
7	30-34	−464.84	<.0001	**<.0001**	−463.72	.0009	**.0002**	.1505	2.243	.1342
8	35-39	−480.52	<.0001	**<.0001**	−478.63	<.0001	**<.0001**	.0597	3.785	.0517
9	40-44	−497.01	<.0001	**.0002**	−496.04	<.0001	**.0056**	.177	1.936	.1641
10*	45-49	−512.55	<.0001	.063	−510.28	<.0001	**.0076**	**.038**	4.523	**.0334**
11	50-54	−520.73	<.0001	.8234	−518.35	<.0001	.0643	**.0325**	4.753	**.0292**
12	55-59	−529.92	<.0001	**.0056**	−525.27	<.0001	.1288	**.0025**	9.309	**.0023**
13	60-64	−528.54	<.0001	**<.0001**	−525.71	<.0001	.8396	**.0185**	5.674	**.0172**
14	65-69	−528.40	<.0001	**<.0001**	−524.73	<.0001	.823	**.0073**	7.339	**.0068**
15	70-74	−527.74	<.0001	**<.0001**	−524.59	<.0001	.2765	**.0132**	6.282	**.0122**
16	75-79	−523.19	<.0001	**<.0001**	−518.21	<.0001	.5581	**.0016**	9.967	**.0016**
17	80-84	−496.91	<.0001	**<.0001**	−492.64	<.0001	.1813	**.0037**	8.550	**.0035**
18	85+	−473.15	<.0001	**<.0001**	−468.35	<.0001	.3123	**.0021**	9.613	**.0019**

Boldface indicates statistical significance.
LL, Log likelihood; *LLR*, log likelihood ratio; *UVI*, ultraviolet index.
*Two age categories when sex switches between significant and nonsignificant roles in Model A.

melanoma in both models; adding UVI*sex interaction significantly improved the model (Table III). The interaction between UVI and sex contributed significantly in determining melanoma risk, as indicated by its significant *P* value (*P* = .0304, Table III). Therefore, sex alone and the interaction between sex and UVI are both crucial.

For the 20 to 44 age group (the major reproductive age group), sex alone played a significant role in both models, whereas the impact of UVI*sex interaction was not significant, as reflected by the *P* values for both the model comparison and the interaction (Table III).

Age 45 to 49 is a transition age, in which sex showed marginally significant impact in model A (*P* = .063) but showed significant impact in model B (*P* = .0076). The interaction between sex and UVI is also significant in this age group (*P* = .038). Therefore, this age group and the age group 15 to 19 are the only 2 groups in which both sex and UVI-sex interaction play significant roles in determining melanoma outcome. For both groups, model B is better than model A, which emphasizes the importance of the interaction.

Sex does not play a role in the age 50 to 54 group in either model. This is consistent with our previous findings: the rate ratio between sexes for this age group is nearly 1.0.[9] When the UVI and sex interaction is taken into consideration, sex is still not a significant contributor (*P* = .064), but the interaction is (*P* = .0325) (Table III).

After age 54, model B was significantly better than model A; therefore, sex alone is no longer a significant risk factor, even though we know that men's rates are higher than women's in these ages. In these older age groups, it is the interaction between sex and UVI that becomes important (Table III).

DISCUSSION AND CONCLUSIONS

The role of sex in melanoma development was well known before, but it was mostly focused on the incidence rate difference at different ages. Here we have revealed a significant interaction between sex and UVI, which has been under-reported. What was more striking is that the interaction between sex and UVI was age dependent. Before age 45, there is no significant interaction between sex and UVI and sex and UVI independently contribute to melanoma risk. After age 49, the UVI and sex interaction played a significant role in melanoma risk, whereas sex itself was no longer significant. These results may suggest that (1) sex plays an independent role in development of early-onset melanoma and (2) sex exhibits a modifying role on UVI impact in melanoma occurring later in life; specifically, female sex exhibited a protective role against ambient UVR exposure.

It is worth noting that the interaction was dependent on age, with 15 to 19 and 45 to 49 years as the 2

switching ages. The age group 15 to 19 is the group of individuals just about to complete pubertal changes and reach their lifetime high sex hormonal levels.[17,18] Meanwhile, this group is also reported to use tanning beds more often than other age groups,[19] There may be a link between tanning bed use and geographic UVI, so it seems that multiple factors may be at play for this particular age group. The 15 to 19 and 45 to 49 age groups are also the exact ages when sex hormones exhibit the most dramatic changes in the human life span.[20] In particular, both estrogen and testosterone levels dramatically increase during the ages of 15 to 19 and they both dramatically decrease in the 45 to 49 year age group. This coincidence may suggest a link of these hormonal changes with melanoma risk, and these changes interact with geographic UVI to affect melanoma development. The role of hormonal impact is further supported by the nonsignificant role of sex for melanomas diagnosed before age 15, when the sexual biologic difference is not as dramatic as at later ages.

For melanomas diagnosed in individuals at an older age, although sex no longer contributes independently to melanoma risk, female sex shows a protective role against UVR. Without age stratification, female sex exhibits an overall protective effect (Table II). These results provide a possible explanation and validation of our previous observation that the incidence rates in women are not significantly associated with UVI in a linear model.[14] In contrast, the incidence rates in men are significantly associated with ambient UVI, and the association levels increase with age.

The limitation of this study is that the interaction between sex and UVI is based on geographic UVR, which may not reflect how much UVR a person receives, which is also difficult to separate from other environmental factors such as temperature and latitude. Confounding factors such as indoor tanning device use cannot be separated from the sex factor, as females are more intent on having tanned skin either through tanning devices or sun bathing.[21] However, females also tend to use significantly more sunscreen.[22-24] Furthermore, from our previous observation, it is known that young female individuals did not show a particularly higher incidence rate for nonmelanoma skin cancer,[9] which is also caused by UVR. Therefore, it is highly likely that it is female sex, and not the sun behavior of females, that contributes significantly to melanoma risk at young ages.

In summary, our results suggest that ambient UVR exposure and sex each contribute to melanoma risk independently for those in whom the disease is diagnosed at a younger age (≤44 years) and that ambient UVR plays a significant role in melanoma risk for those in whom the disease is diagnosed at an older age (≥45 years). However, there is a significant interaction between sex and UVI for melanomas occurring at an older age, manifesting as a protective role of female sex against UV-associated melanoma risk. The significance of these observations warrants further investigations into the mechanism of sex difference and how this difference can be utilized in developing effective prevention strategies.

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SUPPLEMENTAL METHODS

Calculation of age-standardized rates

Age-standardized rates were calculated on the basis of the standard world population 2000-2025 (obtained from the Surveillance, Epidemiology, and End Results website [https://seer.cancer.gov/]).

More on UVI collection

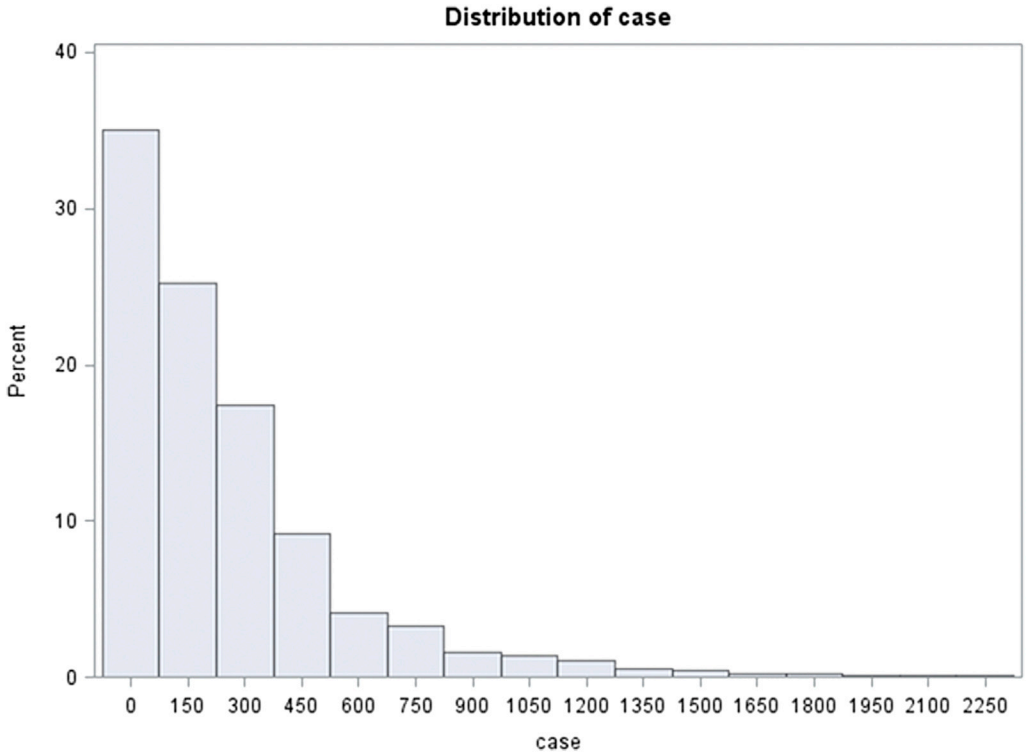
Ultraviolet index (UVI) information was obtained as previously described from local satellite stations (Liu-Smith et al[14]), except for a few areas where no station was located. UVI was estimated for these areas on the basis of the similarity of latitude from another area where a monitoring station was available. Local median latitude was obtained as where the central line lays for that area, without weighing out the area shape.

Statistical Models

As shown in the histogram in Supplemental Fig 1, the case numbers follow a Poisson distribution. The dispersion calculated by maximum likelihood estimation was 2.035 with a 95% Wald confidence interval of 1.888 to 2.169, which is significantly different from 0, suggesting that a negative binomial model was more suitable for parameter estimation. When estimated by the Pearson chi-square method, the data fit well into a negative binomial distribution (data not shown). Log-transformed case number was a dependent variable, and log-transformed population was used as an offset. Scale was defined as deviance. The age category was converted to numerical age by using the midpoint of that category. For example, the numerical age for age category 5 (20-24 years old) is 22.5, and so on.

The base model (model 1) included sex, age, and UVI as independent variables. Next, we added potential interactions among sex, age, and UVI in model 1 and sequentially generated model 2 (with interaction between UVI and sex, UVI*sex), model 3 (UVI*age), and model 4 (age*sex). Model 5 included all three 2×2 interactions.

Model A and model B were also based on the negative binomial regression for each age strata. Model A included only UVI and sex, and model B included UVI*sex interaction as an additional variable.



Supplemental Fig 1. Melanoma. Histogram of case numbers (numbers for each 5-year age category from each registry). Distribution suggested a Poisson distribution.

Supplemental Table I. Parameter estimate from different models using latitude

Model	Variable	Coeeficient	Standard error	Wald 95% confidence intervals		Wald chi-square	Pr > ChiSq	*P* value for model comparison
Model 1	Intercept	−10.149	0.1123	−10.369	−9.929	8162.22	<.0001	
	Latitude	−0.0307	0.002	−0.0346	−0.027	229	<.0001	
	Sex	−0.1374	0.048	−0.2314	−0.044	8.22	.0042	
	Age	0.0631	0.0012	0.0607	0.066	2679.83	<.0001	
	LL	−8867.5						NA
Model 2	Intercept	−10.548	0.1405	−10.823	−10.27	5638.65	<.0001	
	Latitude	−0.0218	0.0028	−0.0273	−0.016	59.82	<.0001	
	Sex	0.6568	0.1856	0.293	1.021	12.52	.0004	
	Age	0.063	0.0012	0.0607	0.065	2711.69	<.0001	
	Latitude*sex	−0.0177	0.004	−0.0256	−0.010	19.56	<.0001	
	LL	−8855.8						<.0001
Model 3	Intercept	−10.86	0.2342	−11.32	−10.40	2150.4	<.0001	
	Latitude	−0.0147	0.0051	−0.025	−0.005	8.51	.0035	
	Sex	−0.1389	0.0477	−0.232	−0.046	8.5	.0036	
	Age	0.0788	0.0048	0.0695	0.0882	272.97	<.0001	
	Latitude*age	−0.0004	0.0001	−0.0006	−0.0001	11.66	.0006	
	LL	−8860.5						<.0001
Model 4	Intercept	−9.6074	0.1222	−9.8468	−9.3679	6182.3	<.0001	
	Latitude	−0.0305	0.002	−0.0343	−0.0267	244.79	<.0001	
	Sex	−1.1911	0.1143	−1.4152	−0.967	108.55	<.0001	
	Age	0.0504	0.0017	0.0472	0.0537	918.54	<.0001	
	Age*sex	0.0233	0.0023	0.0188	0.0278	102.07	<.0001	
	LL	−8808.9						<.0001
Model 5	Intercept	−10.499	0.2476	−10.984	−10.014	1798.35	<.0001	
	Latitude	−0.0109	0.0052	−0.0211	−0.0006	4.34	.0373	
	Sex	−0.4523	0.2052	−0.8546	−0.05	4.86	.0275	
	Age	0.0621	0.0048	0.0528	0.0715	169.7	<.0001	
	Latitude*age	−0.0003	0.0001	−0.0005	−0.0001	6.72	.0096	
	Latitude*sex	−0.016	0.0039	−0.0236	−0.0085	17.35	<.0001	
	Age*sex	0.0229	0.0023	0.0184	0.0273	99.86	<.0001	
	LL	−8794.3						<.0001

ChiSq, Chi-square; *LL*, log likelihood value; *NA*, not available; *Pr*, Pearson; *UVI*, ultraviolet index.