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Association between cutaneous melanoma incidence rates among white U.S. residents and county-level estimates of solar ultraviolet exposure

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Abstract

Background—Recent U.S. studies have raised questions as to whether geographic differences in cutaneous melanoma incidence rates are associated with differences in solar ultraviolet (UV) exposure.

Objectives—To assess the association of solar UV exposure with melanoma incidence rates among U.S. non-Hispanic whites.

Methods—We assessed the association between county-level estimates of average annual solar UV exposure for 1961–1990 and county-level melanoma incidence rates during 2004–2006. We used Poisson multilevel mixed models to calculate incidence density ratios by cancer stage at diagnosis while controlling for individuals' age and sex and for county-level estimates of solar UV exposure, socioeconomic status, and physician density.

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Preliminary findings from this study were presented at the 2010 annual conference of the North American Association of Central Cancer Registries in Quebec City, Quebec, Canada.

CDC Human Subject Institutional Review Board: CDC Human Subject Institutional Review Board (IRB) approval was not required for the analyses in this study because: the study met the requirements of the CDC National Program of Cancer Registries (NPCR); and the NPCR has CDC IRB approval for analyses meeting NPCR requirements.

Results—Age-adjusted rates of early- and late-stage melanoma were both significantly higher in high solar UV counties than in low solar UV counties. Rates of late-stage melanoma incidence were generally higher among men, but younger women had a higher rate of early-stage melanoma than their male counterparts. Adjusted rates of early-stage melanoma were significantly higher in high solar UV exposure counties among men aged 35 or older and women aged 65 or older.

Limitations—The relationship between individual-level UV exposure and risk for melanoma was not evaluated.

Conclusions—County-level solar UV exposure was associated with the incidence of early-stage melanoma among older U.S. adults but not among younger U.S. adults. Additional studies are needed to determine whether exposure to artificial sources of UV exposure or other factors might be mitigating the relationship between solar UV exposure and risk for melanoma.

Keywords

solar ultraviolet rays/adverse effects; melanoma/epidemiology; skin neoplasms/epidemiology; population surveillance; incidence; registries; socioeconomic factors; dermatology/manpower

Previous U.S. studies of melanoma mortality and incidence rates among non-Hispanic whites have shown rates to be higher in the South where solar ultraviolet (UV) exposures are higher.^{1–2} However, results from more recent U.S. studies have suggested that the relationship between geographic-based differences in solar UV exposure and melanoma rates may be attenuated or modulated by other factors.^{3–6} These factors include altitude,⁷ whether Hawaii is included in the analysis,^{2,8} population demographics,¹ the completeness of melanoma case reporting,^{9–10} and the sun-protection behaviors, geographic mobility, risk awareness, and early melanoma detection efforts in the populations studied.¹¹

Studies of the association between melanoma incidence rates and geographic-based differences in solar UV exposure must overcome several additional challenges, including the need for a 30-year history of meteorological data to establish norms, means, and extremes variables¹²; the need for accurate solar UV exposure estimates for small areas; and the need to account for the accumulated effects of lifetime UV exposure.¹³

The National Solar Radiation Database (NSRDB), which has been used to estimate the 30-year Average daily total GLObal solar radiation (AVGLO) exposure for each county in the contiguous United States from 1961 through 1990, can help meet these challenges.¹² The AVGLO values derived from the NSRDB indicate the total amount of solar radiation received on a horizontal surface in a specified area in watt hours per square meter (Wh/m²)¹² and can be used to produce elevation-adjusted estimates of the total annual erythemally weighted UV exposure people might experience at any given location.^{12,14}

Our primary objective in this study was to quantify the association between county-level AVGLO values and cutaneous melanoma incidence rates by stage at diagnosis among non-Hispanic whites in the United States. A secondary objective was to evaluate the extent to which any associations between AVGLO values and these rates might be modified by individual level factors such as age and sex or by area-based factors such as county-level socioeconomic status (SES) and physician density.

METHODS

Data

The melanoma incidence data we assessed were from 42 population-based U.S. cancer registries that participated in the National Program of Cancer Registries (NPCR) and the

Surveillance, Epidemiology, and End Results (SEER) Program from 2004 through 2006, met the high-quality data criteria for the *United States Cancer Statistics* (USCS) report,¹⁵ released county-level incidence data, and were in areas with AVGLO estimates from 1961–1990. The 42 registries were in: Alabama, Arkansas, California, Colorado, Connecticut, Delaware, the District of Columbia, Florida, Georgia, Idaho, Indiana, Iowa, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Michigan, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New Jersey, New Mexico, North Carolina, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Rhode Island, South Carolina, South Dakota, Tennessee, Utah, Vermont, Virginia, Washington, West Virginia, and Wyoming (Figure 1). These registries covered 74.1% of the U.S. population for 2004–2006, and 2,412 (76.8%) of 3,141 U.S. counties.

Our analysis was limited to microscopically confirmed cases of invasive melanoma of the skin in non-Hispanic whites aged 15 years or older. We used SEER Summary Stage 2000 to assign melanoma stage at diagnosis to two categories: early-stage (i.e., localized-stage) and late-stage (i.e., regional- and distant-stages combined).¹⁵

We used NSRDB data¹² adjusted for altitude to determine the mean AVGLO values for each county in the contiguous United States during 1961–1990, and then divided the counties in the contiguous U.S. (n=3,109) into three groups on the basis of their AVGLO values: low AVGLO counties (mean AVGLO values 3,011.7–4,079.8; 1,037 counties); middle AVGLO counties (mean AVGLO values 4,079.9–4,492.2; 1,036 counties); and high AVGLO counties (mean AVGLO values 4,492.3–5,722.5; 1,036 counties). However, we analyzed data only from the 779 low AVGLO counties, 920 middle AVGLO counties, and 713 high AVGLO counties covered by the 42 cancer registries in our study (Figure 1).

We used data from the U.S. Census 2000 to categorize counties by high school education prevalence among residents aged ≥ 25 years (<75%, 75% to < 85%, ≥85%); median household income (<\$35,000, \$35,000 to < \$50,000, ≥ \$50,000); and percentage of residents below the federal poverty level (<10%, 10% to <20%, ≥ 20%). We used the U.S. Census Bureau's *Model-Based Small Area Health Insurance Estimates*¹⁶ (for ages 18 to 64 years, all races, both sexes, and all income levels, in 2006) to categorize counties by percentage of residents with health insurance (≤ 77.0%, 77.1% to 82.9%, ≥ 83.0%), and classifications from the U.S. Department of Agriculture 2003 Rural-Urban Continuum Codes (RUCC)¹⁷ to categorize counties as metropolitan [RUCC 1–3], non-metropolitan with urban populations [RUCC 4–7], or rural [RUCC 8–9]. We obtained the numbers of dermatologists, internists, and general practice physicians in each county in 2004, 2005, and 2006 from the U.S. Health Resource and Services Administration Area Resource File¹⁸ and estimated the number of physicians in each category per 10,000 population by dividing the average number of physicians per year by the 2000 U.S. Census population for each county.

Analyses

Patient age at diagnosis was available in 5-year intervals. To smooth the variation in age-specific incidence rates, we calculated age-specific rates using 15-year age groups that advanced by 5 years (e.g., 50–64 years, 55–69 years, 60–74 years). The rate for each 15-year age group was the sum of the cases for that group divided by the sum of the population denominators for the same age group.

Using SEER Stat software,¹⁹ we computed direct age-adjusted melanoma incidence rates and rate ratios with 95% confidence intervals by AVGLO exposure category and melanoma stage at diagnosis. We expressed rates as cases per 100,000 residents and standardized rates to the 2000 U.S. Census standard population.

We used Generalized Linear Mixed Models (SAS PROC GLIMMIX, version 9.2, SAS Institute, Inc., Cary, NC)²⁰ to calculate Poisson multilevel mixed models of incidence rates for melanoma cases in the early- and late-stage at diagnosis categories. For these analyses, we divided county residents into three age groups (15–34 years, 35–64 years, and 65 years or older), treated the numbers of melanoma cases in each county by sex and by age group (hereafter referred to as analysis cells) as dependent variables, and adjusted the models for the number of expected cases. To reduce potential confounding by age or sex, we used age- and sex-specific rates for all states to estimate the number of expected cases for the three age groups. The data we used in these analyses had a hierarchical multilevel structure, with analysis cells nested within counties, which were nested within states. We assumed analysis cell counts to be independent Poisson variables, conditional on random effects at the state and county level, and on fixed effects at the county and analysis cell levels.²⁰

Independent variables included both categorical and continuous types. Categorical variables were county-level AVGLO, education, poverty, household income, health insurance, and rural-urban status described previously. Continuous variables were county-level physician density measures for dermatologists, internal medicine specialists, and general practitioners. To provide a measure of state-to-state variation in incidence rates, we included the state of residence at the time of diagnosis as a random effect. To provide a better fit of models to the data, we also included a county-based random effect measure in the final models, which we calculated using latitude and longitude coordinates for the center (centroid) of each county. We interpreted the exponentials of the coefficients estimated in the models as incidence density ratios (IDRs). This measure of effect is the ratio of the numbers of observed cases divided by the number of expected cases in a group of interest to the numbers of observed cases divided by the number of expected cases in a referent group.

In early-stage models, we stratified results by sex, and then by age group and AVGLO categories; this approach helped us evaluate a possible three-way sex-age-AVGLO interaction. In late-stage models, we stratified results only by sex and by AVGLO categories because we detected no sex-age-AVGLO interaction for late-stage melanoma.

We used F statistics to determine whether fixed effects were significant and t-statistics to determine whether random effects were significant (both at $p < 0.05$). We used 95% confidence intervals to determine whether sex- and age-specific IDRs for middle and high AVGLO counties were significantly different from low AVGLO counties (the reference group).

RESULTS

We identified 120,037 microscopically confirmed cases of invasive melanoma among non-Hispanic whites aged ≥ 15 years of age who resided in the study area during 2004–2006.

High AVGLO counties generally had higher age-specific incidence rates for both early- and late-stage melanoma than low AVGLO counties (Figure 2). Overall, among people younger than age 40, the rate of early-stage melanoma was higher among women, but among those 40 or older, the rates were higher among men (Figure 2). Rates of late-stage melanoma were higher among men than among women at all ages and in all AVGLO categories.

Age-adjusted incidence rates for both stage at diagnosis categories were higher in high AVGLO counties than in low AVGLO counties; about 80% of all cases were diagnosed at the early stage (Table I).

For adjusted, early-stage melanoma incidence rates, the state of residence at time of diagnosis was significant ($p < 0.05$) in 22 registries. The rate of early-stage melanoma was

higher in high-AVGLO counties than in low AVGLO counties among men aged 35 or older and among women aged 65 or older (Table II).

For adjusted, late-stage melanoma incidence rates, the state of residence at time of diagnosis was significant in only two registries. The rate of late-stage melanoma was higher among women in low AVGLO counties but not associated with county AVGLO exposure among men (Table II).

Details on our analysis of SES factors are not shown in tables, but we found that early stage melanoma incidence rates were higher in counties with higher education levels, higher household income levels, lower poverty rates, and higher rates of health insurance coverage, and also higher in metropolitan and urban counties than in rural counties. None of these SES factors were associated with the rate of late-stage melanoma.

Physician density was positively associated with early-stage melanoma incidence rates, but not with late-stage melanoma incidence rates (Table III).

DISCUSSION

After controlling for all covariates, we found county-level estimates of solar UV exposure to be positively associated with rates of early-stage melanoma among men aged 35 or older and among women aged 65 or older, but negatively associated with late-stage melanoma rates among women aged 15 or older and not significantly associated with rates of late-stage melanoma among men aged 15 or older. We have no explanation for the different relationships observed between AVGLO exposure and melanoma incidence in the various sex and age categories.

Our results indicate the importance of conducting separate analyses for early-stage and late-stage melanoma cases. For example, the model for early-stage cases had a sex-age-AVGLO exposure interaction, whereas the model for late-stage cases did not. Similarly, the state of residence at time of diagnosis was a significant effect in Poisson models for early-stage melanoma in about half of the registries used in our study, but it was a significant effect for late-stage melanoma in only 2 of the 42 registries. Possible reasons for the differences include differences by state in residents' sun protection behaviors and genetics, the thoroughness of melanoma case reporting, and the prevalence of geographic features (such as beaches or mountains) that could affect residents' UV exposure. We were unable to explore these possibilities.

Our adjusted findings that county-level estimates of solar UV exposure were positively associated with the rates of early-stage melanoma results in older adults but not among younger adults suggests that artificial sources of UV exposure or other factors might be mitigating the melanoma risk difference between younger adults in high AVGLO counties and those in low AVGLO counties.^{21–22}

Our finding that the incidence rate of early-stage melanoma was positively associated with county level SES and physician density could be explained by higher SES individuals being more likely to go on vacations resulting in sunburn or to frequent tanning salons, as well as to live in areas with relatively high physician density.^{23–25}

Our finding that the incidence rate for late-stage melanoma was not associated with county-level SES was in conflict with results of a previous study showing that education level was an important predictor of melanoma prognosis, defined as the melanoma mortality ratio to incidence ratio and measured using census tract level data from 1988 to 1993 in 9 SEER registries.²⁶ The conflict might be accounted for by factors such as differences in: the

outcome (incidence rates versus ratio of mortality to incidence ratios), the size of the geographic unit of analysis (county versus census tract), the number of registries (42 versus 9), the study populations (Hawaii excluded versus Hawaii included), and the melanoma incidence years of diagnosis (2004–2006 versus 1988–1993).

Our study used different time periods for solar UV exposure and melanoma incidence. Use of the 2004–2006 time period for melanoma incidence enabled an expanded US geographic area to be included in our study, because a larger number of counties released county-level incidence data that met the high-quality data criteria for *United States Cancer Statistics* reporting in 2004–2006 than in earlier time periods.¹⁵ Analysis of the relationship between solar UV exposure from earlier time periods and melanoma incidence in more recent time periods is of potential interest because melanoma incidence is associated with the accumulated effects of lifetime UV exposure.¹³ Use of a 30-year period (1961 to 1990) for exposure also provides more accurate solar UV exposure estimates for US counties than possible with shorter time periods.¹² Furthermore, adding another decade of solar UV data would not add to the quality of our estimates of potential solar UV exposure, because the annual average measures of solar UV exposure did not vary significantly over the three decades considered.¹²

Our study has five notable limitations. First, the accuracy of our findings for early-stage melanoma could have been affected by incomplete reporting of thinner melanomas or by regional differences in diagnostic scrutiny for melanoma.^{9–10,15,27}

Second, although the 42 cancer registries whose data we used cover close to three-fourths of the U.S. population, several missing registries with relatively large populations were in locations classified as having either high or low AVGLO exposure, and their exclusion may have affected our findings.^{2,8}

Third, although AVGLO exposure values can be estimated for census tract or even smaller geographic units, our analysis had to be based on less precise county-level data because melanoma incidence data were only available at the county level. Our analyses also did not account for individual variations in sun exposure protection behaviors or use of tanning beds or other artificial UV sources or for subjects' residential history prior to the time of their melanoma diagnosis. We analyzed relationships between incidence rates that were geographically aggregated to the county-level and solar UV exposures that were geographically aggregated to the county level. Caution is needed when drawing inferences about individuals based on the aggregate data for a group.²⁸ Disaggregating data may reveal statistical relationships that are different from those at the aggregated level; geographers refer to this situation as the *ecological fallacy*.²⁸ In our county-level analysis, there is no guarantee that the individuals with the highest risk of melanoma are also those with the highest solar UV exposures, or vice-versa. If our analysis had been based on individual lifetime solar UV estimates³² that accounted for the timing, amount, and nature of the exposure for each case, then we might have observed different results.

Fourth, our Poisson regression results may have been affected by small melanoma case counts for some of the county-level analysis cells and by correlations between county location, county solar UV exposure values, and state random effects.

Finally, our study did not include details on the various ethnic and ancestry categories included within non-Hispanic whites in the United States, and geographic clustering of individuals with higher levels of genetic risk for melanoma could have affected our results.^{29–31}

CONCLUSIONS

We found that the incidence rate of early-stage melanoma among men aged 35 or older and women aged 65 or older was significantly higher in counties ranked in the highest third for overall solar UV exposure than in counties ranked in the lowest third, but that the rates among younger men and women did not differ significantly by county UV exposure classification. This lack of difference in melanoma incidence by county-level UV exposure raises questions about whether exposures to artificial sources of UV radiation or other factors might be mitigating the association between solar UV exposure and melanoma risk. Further analyses based on individual-level information will be needed to assess the extent to which such factors actually do mitigate this association. A challenge for future studies will be how to replace the relatively crude county-level estimates of solar UV exposure that we used in our study with more precise individual-level estimates that account for the timing, amount, and nature of the exposure.³²

Acknowledgments

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Abbreviations used

AVGLO	Average daily total GLObal solar radiation
IDR	incidence-density ratio
SES	socioeconomic status
UV	ultraviolet
Wh/m²	watt hours per square meter

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Figure 1. County-level AVerage daily total GLObal solar radiation (AVGLO) exposure in watt-hours per square meter for the study area, 1961–1990.¹²

Figure 2.

Early- and late-stage age-specific melanoma incidence rates (per 100,000) among non-Hispanic whites, by sex and AVerage daily total GLObal solar radiation (AVGLO) classification for county of residence, 2004–2006. Melanoma incidence rates are for 15-year age groups that advance by 5 years. Low AVGLO counties had mean AVGLO values ≤ 4079.9 watt-hours per square meter (Wh/m^2); middle AVGLO counties had mean AVGLO values 4079.9 to 4492.2 Wh/m^2 ; and high AVGLO counties had mean AVGLO values ≥ 4492.3 Wh/m^2 .

Table I

Age-adjusted incidence rates of microscopically confirmed invasive cutaneous melanoma among non-Hispanic whites aged 15 years or older, reported by 42 population-based cancer registries, 2004–2006, by sex, cancer stage, and AVGLO classification for county of residence.*

Category	Cases	Rate (per 100,000 population)*	Rate ratio (95% CI)
Males			
High AVGLO counties			
All cases	26,185	40.2 [†]	1.22 (1.20, 1.24)
Early stage	20,989	32.2 [†]	1.28(1.25, 1.30)
Late stage	3,796	5.8 [†]	1.19(1.14, 1.25)
Middle AVGLO counties			
All cases	15,507	35.1 [†]	1.07 (1.04, 1.09)
Early stage	11,925	26.9 [†]	1.07 (1.04, 1.09)
Late stage	2,332	5.3 [†]	1.08 (1.03, 1.14)
Low AVGLO counties			
All cases	26,913	32.9	Ref
Early stage	20,686	25.2	Ref
Late stage	3,986	4.9	Ref
Females			
High AVGLO counties			
All cases	17,885	25.8 [†]	1.07 (1.04, 1.09)
Early stage	14,896	21.7 [†]	1.10 (1.08, 1.13)
Late stage	2,033	2.8 [†]	1.09(1.03, 1.16)
Middle AVGLO counties			
All cases	11,548	23.5 [†]	0.97(0.95, 0.99)
Early stage	9,395	19.2	0.98 (0.95, 1.00)
Late stage	1,236	2.4	0.95 (0.88, 1.02)
Low AVGLO counties			
All cases	21,999	24.2	Ref
Early stage	17,701	19.7	Ref
Late stage	2,440	2.5	Ref

CI, confidence interval; AVGLO, AVerage daily total GLObal solar radiation exposure in watt-hours per square meter (Wh/m²); low AVGLO counties had mean AVGLO values < 4079.9 Wh/m²; middle AVGLO counties had mean AVGLO values 4079.9 to 4492.2 Wh/m²; and high AVGLO counties had mean AVGLO values ≥ 4492.3 Wh/m².

* Age-adjusted to the 2000 U.S. Standard Population for U.S. residents aged 15 years or older.

[†] Rate is significantly different (p<0.05) from the corresponding rate in the low AVGLO reference group (Ref).

Table II

Multilevel model adjusted melanoma incidence density ratios for middle and high AVGLO counties versus low AVGLO counties, by sex, age group, and stage at diagnosis among non-Hispanic whites aged 15 years and older, reported by 42 population-based cancer registries, 2004–2006.

		Middle vs. Low AVGLO counties	High vs. Low AVGLO counties
Sex	Age group (years)	IDR (95% CI)*	IDR (95% CI)*
Early Stage			
Female	15–34	0.998 (0.922, 1.080)	0.919 (0.843, 1.002)
Female	35–64	0.997 (0.945, 1.053)	0.983 (0.918, 1.052)
Female	≥ 65	1.008 (0.948, 1.073)	1.076 (1.0002, 1.157) [†]
Male	15–34	0.954 (0.854, 1.066)	1.067 (0.959, 1.188)
Male	35–64	1.108 (1.050, 1.168) [†]	1.156 (1.080, 1.237) [†]
Male	≥ 65	1.099 (1.041, 1.160) [†]	1.151 (1.076, 1.232) [†]
Late Stage			
Female	≥ 15	0.870 (0.788, 0.961) [†]	0.840 (0.740, 0.952) [†]
Male	≥ 15	0.999 (0.915, 1.090)	0.913 (0.810, 1.030)

IDR, incidence density ratio; CI, confidence interval; AVGLO, AVerage daily total GLObal solar radiation exposure in watt-hours per square meter (Wh/m²); low AVGLO counties had mean AVGLO values < 4079.9 Wh/m²; middle AVGLO counties had mean AVGLO values 4079.9 to 4492.2 Wh/m²; and high AVGLO counties had mean AVGLO values ≥ 4492.3 Wh/m².

* IDRs are adjusted for age, sex, percent at least high school education, percent persons below poverty, median household income, rural urban location, small area health insurance estimates, physician density, and county and state random effects.

[†] IDR is significantly different (p<0.05) from the corresponding IDR in the low AVGLO reference group.

Table III

Multilevel model adjusted melanoma incidence density ratios by stage at diagnosis and physician density in the county of residence, among non-Hispanic whites aged 15 years or older, reported by 42 population-based cancer registries, 2004–2006.*

Physicians per 10,000	IDR (95% CI)
Early Stage	
Dermatologists	1.137 (1.101, 1.175) [‡]
Internal Medicine	1.007 (1.002, 1.012) [‡]
General Practitioner	1.008 (1.002, 1.013) [‡]
Late Stage	
Dermatologists	1.009 (0.922, 1.105)
Internal Medicine	0.999 (0.988, 1.011)
General Practitioner	1.011 (0.999, 1.024)

IDR, incidence density ratio; CI, confidence interval;

* The results shown in Table III are additional effects for the models calculated in Table II.

[†] IDRs are adjusted for age, sex, AVerage daily total GLObal solar radiation exposure in watt-hours per square meter (Wh/m²) (AVGLO), percent at least high school education, percent persons below poverty, median household income, rural urban location, small area health insurance estimates, physician density, and county and state random effects.

[‡] 95% CI does not include 1.0.