Published in final edited form as:
*Cancer Epidemiol Biomarkers Prev*. 2014 October ; 23(10): 2145–2152. doi: 10.1158/1055-9965.EPI-14-0431.

# Sun Exposure and Melanoma Survival: A GEM Study

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## Abstract

**Background—**We previously reported a significant association between higher ultraviolet radiation exposure before diagnosis and greater survival with melanoma in a population-based study in Connecticut. We sought to evaluate the hypothesis that sun exposure prior to diagnosis

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was associated with greater survival in a larger, international population-based study with more detailed exposure information.

**Methods—**We conducted a multi-center, international population-based study in four countries – Australia, Italy, Canada and the United States – with 3,578 cases of melanoma with an average of 7.4 years of follow-up. Measures of sun exposure included sunburn, intermittent exposure, hours of holiday sun exposure, hours of water-related outdoor activities, ambient UVB dose, histological solar elastosis and season of diagnosis.

**Results—**Results were not strongly supportive of the earlier hypothesis. Having had any sunburn in one year within 10 years of diagnosis was inversely associated with survival; solar elastosis – a measure of lifetime cumulative exposure – was not. Additionally, none of the intermittent exposure measures – water related activities and sunny holidays - were associated with melanoma-specific survival. Estimated ambient UVB dose was not associated with survival.

**Conclusion—**Although there was an apparent protective effect of sunburns within 10 years of diagnosis, there was only weak evidence in this large, international, population-based study of melanoma that sun exposure prior to diagnosis is associated with greater melanoma-specific survival.

**Impact—**This study adds to the evidence that sun exposure prior to melanoma diagnosis has little effect on survival with melanoma.

### Keywords

Melanoma; survival; sun exposure

## INTRODUCTION

Ultraviolet radiation exposure (UVR) is the major environmental risk factor for the development of melanoma (1) with intermittent UVR exposure, including sunburn, generally the measure of sun exposure most strongly associated with the development of melanoma (2–3). In a Connecticut population-based study of 650 melanoma cases followed for an average of five years, Berwick et al. (4) reported that several measures of UVR prior to the diagnosis of melanoma were inversely associated with mortality from melanoma, suggesting that something about sun exposure, possibly its role in Vitamin D production, was limiting cancer progression. Subsequently, Newton-Bishop and colleagues in a UK study of 872 melanoma patients (5) reported that serum vitamin D levels were higher among those with better overall survival, and Rosso and colleagues in a European study of 260 melanoma patients (6) found that melanoma patients with more sunny vacations prior to diagnosis had better melanoma-specific survival. Laboratory studies have shown that vitamin D suppresses tumor proliferation (7) and suggest that increased vitamin D levels might keep a melanoma “in check”. To test the hypothesis that increased sun exposure prior to diagnosis is associated with improved survival from melanoma, we evaluated measures of solar UVR exposure prior to diagnosis in 3,578 incident melanoma patients in the Genes, Environment and Melanoma study (GEM), an international, population-based study (8).

# METHODS

## Subjects

A detailed description of the methods used in this study is available elsewhere (9). Briefly, this multicenter, international population-based study was conducted in four countries through eight population-based tumor registries---in Australia in the states of New South Wales and Tasmania, in Italy in the province of Piedmont, in Canada in the provinces of British Columbia and Ontario, and in the United States in the state of New Jersey, a 39-county area of North Carolina, two Southern California cancer registry populations (the Orange County Registry and the San Diego/Imperial Organization for Cancer Control), and through a hospital-based registry in the state of Michigan.

Institutional review board approval was obtained from all centers and written informed consent was obtained prior to interview. We interviewed 2,372 patients with incident first primary melanoma cases and 1,206 with incident multiple primary cases. Of the 1,206 with multiple primary cases, 96 had been first ascertained with single primaries. Single primary melanoma cases were diagnosed in 2000 and multiple primary cases from 1998 (British Columbia, California, New Jersey and Tasmania) or 2000 (New South Wales, North Carolina and Ontario) to 2003.

The overall participation rate was 54 percent for individuals completing all aspects of the study and submitting a DNA sample.

## Data Collection

A structured questionnaire administered by telephone assessed basic demographics, phenotypic characteristics, family history of cancer, recreational and occupational sun exposure at each decade of life, sunbed use, changes in sun-related behavior after a melanoma diagnosis, and a lifetime residential history. Nevi on the back were self-assessed using a set of photos and by reference to charts showing different patterns of nevi and freckles as previously described (2, 9).

## UVR Exposure Measures

We evaluated effects on survival of measures of UVR exposure in various periods before diagnosis.

**Sunburns—**Individuals reported whether they had been burned severely enough to have pain or blisters for two or more days in a specified year in the 10 years before diagnosis. This was coded as “once or more” or “never”.

**Solar Elastosis—**Solar elastosis, an indicator of sun exposure accumulated over a lifetime (10), was evaluated on histopathological slide review as absent or present. Slides from 2,781 (78%) subjects were reviewed by expert dermatopathologists (LF, KB, PG) to standardize pathologic criteria and add parameters that community pathology laboratories often do not report, such as solar elastosis. Inter-reviewer reliability for solar elastosis was assessed as very good (Kappa = 0.65).

**Intermittent Sun Exposure—**In a previous GEM analysis, two variables were considered to represent intermittent sun exposure – hours of holiday sun exposure in a place sunnier than usual residence and hours of water-related outdoor activities (2). These measures for one year in the most recent decade were categorized into quartiles based on the distribution among the entire population and ranked from low [quartile one] to high [quartile four].

**UVB Radiation Dose—**Individual residential histories were coded for latitude, longitude and altitude from birth to age at diagnosis, and then ambient UVB irradiances calculated for each decade of age from records of satellite measurements of irradiance at the earth's surface as un-weighted wavelength integrated spectral irradiance between 280 and 320 nm. UVB was used in analyses as this wavelength is thought to be the most effective in inducing serum vitamin D levels. Details of the calculations are available in Thomas et al. (10). Ambient UVB levels in the decade of life that included the melanoma diagnosis, at age 10 and over the lifetime (at each decade) were multiplied by the reported time spent outdoors on weekends and weekdays in the same period and categorized into quartiles based on the distribution among the entire population.

**Season of Diagnosis—**Diagnoses were classified by season, with data pooled for summer (December to February in the Southern hemisphere and June–August in the Northern), autumn (March–May in the Southern hemisphere and September–November in the Northern), winter (June–August in the Southern hemisphere and December–February in the Northern), and spring (September–November in the Southern hemisphere and March–May in the Northern).

## Follow-up for Survival

Patient follow-up for vital status was complete through 2007 except in British Columbia and Turin, where vital status was complete through 2008. Date and cause of death seven years after diagnosis were obtained from National Death Indexes, cancer registries and municipal records. We analyzed an average of 7.4 years of melanoma-specific survival. Individuals were classified as "died of melanoma", "died of other cause" and "alive at the end of follow up". An event was considered death due to melanoma. Among patients with multiple primaries, Breslow thickness (see Supplementary Tables 1–3) and anatomic site for the thickest of their lesions were used in statistical models.

## Data Analysis

Cox proportional hazards models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for associations of categories of each exposure variable with melanoma outcome. Time to death from melanoma from diagnosis for those with single primaries or the most recent melanoma for those with multiple primaries was the outcome. Those who died of other causes or who were still alive at follow up were censored in this analysis.

Age at diagnosis, sex, recruitment center, education level, and anatomic site were potential confounders of the association of sun exposure measures and melanoma survival. We found

that there was no difference in effects of sun exposure measures and survival by primary status and therefore included both single and multiple primary melanomas in analyses in order to improve precision and included an indicator variable for primary status in all models. Kricker et al. (11) previously reported that there was no survival difference between multiple and single primaries in GEM. A time-dependent covariate was used for the 96 patients who developed a second primary during the study follow up period. Pigmentary characteristics, prior history of non-melanoma skin cancer and family history of melanoma were assessed but found not to be potential confounders of sun exposure measures in relation to survival. Stratified analyses were conducted to determine if any effect of sun exposure measures on risk of death from melanoma was modified by *MC1R* status (with or without "red hair color" variants D84E, R151C, R160W, and D294H), ability to tan (good and poor) and propensity to sunburn (high and low). Likelihood ratio tests for heterogeneity were used to evaluate significance of any apparent effect modification. Tests for linear trend were performed for ordered categorical variables. All tests were two-sided and $P < 0.05$ was considered statistically significant. All data were analyzed using SAS 9.3 (Cary, NC).

## RESULTS

Of the 3,578 eligible individuals diagnosed with melanoma in this study (2,007 males and 1,571 females), 563 died by the end of follow up (15.7%): 255 (7.1%) from melanoma and 308 (8.6%) from other causes.

Survival analyses are presented as baseline models, with hazard ratios adjusted for center, age, sex, primary status and the time-dependent covariate, and as fully adjusted models, which included the above variables as well as others significantly associated with survival: educational level, and anatomic site.

### Clinical and Host Characteristics and Melanoma-Specific Survival

Anticipated associations for host and clinical characteristics were seen (Table 1). Primary status was not associated with hazard of death from melanoma in the fully adjusted model. Women had a lower risk of dying from melanoma in both the baseline model ($P < 0.001$) and the fully adjusted model ($P = 0.0002$). The hazard of death increased with increasing age (fully adjusted HR 1.02 for each year of age, 95% CI =1.01 to 1.03, $P < 0.0001$). Melanomas on the arms were at lowest risk for poor survival relative to melanoma of the head and neck (fully adjusted HR 0.47, 95% CI = 0.31 to 0.71, $P = 0.003$). Relative to superficial spreading melanoma, the fully adjusted HR for lentigo maligna melanoma was decreased (HR 0.57, 95% CI = 0.33 to 0.98, $P = 0.04$). Breslow thickness (fully adjusted HR 13.79, 95% CI =9.12 to 20.84, for thickness of 4.00 mm or higher relative to thickness of less than 1.00 mm) was strongly and significantly associated with poor prognosis ($P < 0.001$). Similar to most other studies, those with more education had a significantly reduced hazard of dying from melanoma (fully adjusted HR 0.56, 95% CI = 0.40 to 0.78, $P = 0.0005$). Having a family history of melanoma (fully adjusted HR 0.85, 95% CI = 0.58 to 1.24, $P = 0.39$) or a prior history of non-melanoma skin cancer (fully adjusted HR 0.93, 95% CI = 0.71 to 1.23, $P = 0.63$) did not affect the hazard of dying from melanoma.

**Recent Sun Exposure—**We found a reduced HR of melanoma death with one or more sunburns in a year in the decade before diagnosis (fully adjusted HR 0.27, 95% CI = 0.09, 0.85, $P = 0.03$, Table 2). Other sun exposure variables in the decade before diagnosis, including holiday sun hours in a place sunnier than usual residence and hours of water-related activities and estimated UVB dose, and season of diagnosis were not significantly associated with survival from melanoma in either the baseline or the fully adjusted models.

**Early Life Sun Exposure—**We found a significant trend for increasing melanoma mortality with increasing UVB dose at age 10, (fully adjusted HR 1.49, 95% CI = 0.97, 2.30, $P = 0.03$) for the highest quartile compared to the lowest. Other sun exposure variables in early life were not significantly associated with survival from melanoma (Table 3).

**Lifetime Average Annual Sun Exposure—**None of the lifetime cumulative or annual average sun exposure measures were associated either positively or negatively with melanoma-specific survival (Table 4). Solar elastosis was not associated with an increased risk of dying from melanoma in the baseline or the fully adjusted model (HR 0.74, 95% CI 0.52, 1.07, $P = 0.11$). Lifetime annual average levels of holiday sun hours in a place sunnier than usual residence, water related activities and estimated solar UVB dose were also not significantly associated with melanoma-specific survival (Table 4).

### Stratified Analyses

There was little evidence that any association of sun exposure variables and hazard of death from melanoma varied among categories of *MC1R* status, ability to tan and propensity to burn in relationship to melanoma survival (data not shown).

## DISCUSSION

This study of 3,578 highly annotated patients with melanoma shows the expected associations of host characteristics and clinical variables with survival, but provides only a little support for our previous study in Connecticut where sun exposure prior to diagnosis was inversely associated with melanoma survival, such that individuals with higher levels of intermittent sun exposure, presence of solar elastosis and any sunburns prior to diagnosis had better survival. The present study found only an inverse association of sunburns within the 10 years prior to diagnosis with survival from melanoma. Lifetime sunburn history was not associated with survival with melanoma, which is opposite to the finding in the Connecticut study.

Analytic studies of sun exposure and melanoma survival are few. There are differences of study design and study population among the several studies that show an inverse association with either solar UVB or circulating serum vitamin D and survival compared to the present study. Lesions were generally somewhat deeper in the Connecticut study with a mean thickness of 1.81 mm (median 0.81 mm) versus 1.30 mm (median 0.78mm) in this study. This difference is indicative of a general trend to diagnose thinner lesions over time (12). The inclusion of Breslow thickness in the fully adjusted model did not materially modify associations in models without its inclusion (Supplementary Tables 1–3). It is important to note that because this study is population-based, it includes many individuals

with very thin melanomas and hence high overall survival. Such population-based studies are critical for public health recommendations, but any particular effects of lifestyle on survival would be most relevant for the more selected group of people whose melanoma characteristics place them at a higher likelihood of mortality from melanoma.

In the Rosso et al. (6) study, the population from Turin, Italy, was quite small. The major variable associated with improved survival with melanoma was number of holidays to sunny places; it is possible that this variable is confounded with socioeconomic status, which has been found to be inversely associated with hazard of death from melanoma in three studies (13–15).

In the Newton-Bishop et al. (5) study, measures of circulating serum vitamin D were positively associated with relapse-free survival and lower Breslow thickness at diagnosis. This study did not look at melanoma-specific survival, but rather overall survival. Additionally, only individuals with tumors greater than 0.75 mm were included. These results differ from our studies in Connecticut and the present GEM study that both focus on melanoma-specific survival and inclusion of all tumors unrestricted by Breslow thickness. We have evaluated overall survival, however, and found that several measures of intermittent sun exposure prior to diagnosis—UVB dose in quartiles ($P$ for trend = 0.004); hours spent in water-related activities ($P$ for trend = 0.01) and hours of holiday sun exposure ($P$ for trend = 0.03) --- are significantly and inversely associated with survival (Supplementary Table 4). Our data indicate a possible impact of sun exposure on overall survival; however, this study was not designed to evaluate deaths other than melanoma.

Several limitations deserve note, particularly the potential for misclassification in recalled sun exposure. Because the “dose” information relies on reported hours of sun exposure multiplied by the ambient exposure, there is the potential for misclassification that is likely non-directional and would bias results to the null. Additionally, although sunburn is likely subject to recall bias (16), the fact that sunburn represents overexposure to the sun, whereas exposure to high ambient levels of UV is modified by behaviors and phenotype, may make the single finding that sunburn prior to diagnosis is “protective” more salient. Caution is necessary in interpreting that finding due to the very small number of deaths in the group experiencing sunburn (n=4). Misclassification could also result from differences among centers in non-UV sun related behaviors that might affect mortality in comparison to previous single center studies where more uniform non-UV behaviors factors might be more uniform.

Another concern lies with the use of death certificates for verification of mortality as death certificates are sometimes misclassified (17). Each of the centers in this study had high quality identification of deaths, using death certification, such as the National Death Index in the United States and Australia and the Provincial Cancer Registries in Canada. In Italy, deaths were verified by linking to the municipal rosters. If in fact a patient died from a metastasis from his melanoma but was classified as dying from another cancer, such as lung cancer, then our statistical power will have been reduced. Furthermore, it is noted that deaths from melanoma continue to occur over a relatively long period of time, and we have

survival information for 7.4 years, so that a longer follow up period may produce somewhat different results.

Many studies have demonstrated positive associations between solar UV exposure at season of diagnosis and survival from different cancers. Results are mixed although the majority of studies demonstrate that those cancers diagnosed in the fall, when circulating serum vitamin D levels are generally the highest, have better prognosis than those diagnosed in other seasons. For melanoma, one study found higher survival in patients diagnosed in summer or fall (18) and one did not (19); both were from Australia.

Our study's strengths include the large number of participants, the variety of latitudes, the relatively long follow up, a reliable sun exposure questionnaire (20–21), the ability to control for confounders, and the extensive pathologic review of cases.

In conclusion, this study provides only weak evidence that high levels of sun exposure prior to diagnosis have a benefit for melanoma survival.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Financial Support: This work was supported by the National Institutes of Health: U01 CA 83101, R01 CA112524, R01 CA112524-05S2, and K05 CA13165, to M. Berwick; R01 CA112243, R01 CA112243-05S1, P30 CA118100 and P30 ES010126 to N. Thomas, and Michael Smith Foundation for Health Research Infrastructure Award to R. Gallagher. The National Center for Atmospheric Research is sponsored by the National Science Foundation

The study was conducted by the GEM Study Group:

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*Cancer Epidemiol Biomarkers Prev*. Author manuscript; available in PMC 2015 October 01.

**Table 1**

Host and clinical factors associated with melanoma survival.

| Variable | Level | No. in Study | No. Died from Melanoma | Baseline Model** HR (95% CI) | Fully Adjusted Model+ HR (95% CI) |
|---|---|---|---|---|---|
| | | 3578 | 255 | | |
| Primary Status | Single | 2372 | 152 | 1.00 | 1.00 |
| | Multiple | 1206 | 103 | 0.99 (0.75, 1.32) | 1.03 (0.78, 1.37) |
| *P*-value | | | | 0.98 | 0.83 |
| Sex | Male | 2007 | 184 | 1.00 | 1.00 |
| | Female | 1571 | 71 | 0.56 (0.43, 0.75) | 0.56 (0.42, 0.76) |
| *P*-value | | | | <0.001 | 0.002 |
| Age at Diagnosis | Per Year | | | 1.03 (1.02, 1.04) | 1.02 (1.01, 1.03) |
| *P*-value | | | | <0.001 | < 0.001 |
| Anatomic Site | Head & Neck | 578 | 77 | 1.00 | 1.00 |
| | Trunk | 1585 | 107 | 0.54 (0.40, 0.73) | 0.53 (0.39, 0.73) |
| | Arms | 666 | 34 | 0.47 (0.31, 0.71) | 0.47 (0.31, 0.71) |
| | Legs | 749 | 37 | 0.51 (0.33, 0.77) | 0.51 (0.34, 0.78) |
| Histology | SSM | 2302 | 106 | 1.00 | 1.00 |
| | NM | 333 | 70 | 4.27 (3.13, 5.81) | 3.74 (2.72, 5.14) |
| | LMM | 366 | 18 | 0.85 (0.51, 1.41) | 0.57 (0.33, 0.98) |
| | ALM | 16 | 3 | 8.99 (3.62, 22.36) | 9.90 (3.87, 25.38) |
| | NOS | 496 | 40 | 1.95 (1.33, 2.86) | 1.85 (1.26, 2.73) |
| | Other | 65 | 18 | 4.51 (2.59, 8.15) | 3.04 (1.65, 5.61) |
| Breslow thickness | 0.01–1.00 | 2228 | 45 | 1.00 | 1.00 |
| | 1.01–2.00 | 727 | 79 | 5.33 (3.69, 7.70) | 5.13 (3.53, 7.41) |
| | 2.01–4.00 | 361 | 75 | 10.06 (6.92, 14.60) | 9.65 (0.62, 14.07) |
| | >4.00 | 175 | 52 | 15.03 (10.02, 22.53) | 13.81 (9.13, 20.88) |
| | Missing | 87 | 4 | | |
| *P*-value for trend | | | | <0.001 | <0.001 |
| Education | < College | 2415 | 203 | 1.00 | 1.00 |
| | College + | 1133 | 47 | 0.56 (0.40, 0.78) | 0.69 (0.49, 0.97) |
| *P*-value | | | | 0.0006 | 0.03 |

| Variable | Level | No. in Study | No. Died from Melanoma | Baseline Model** HR (95% CI) | Fully Adjusted Model+ HR (95% CI) |
|---|---|---|---|---|---|
| Family history of melanoma | None | 2953 | 212 | 1.00 | 1.00 |
| | Present | 551 | 31 | 0.82 (0.56, 1.21) | 0.85 (0.58, 1.24) |
| | Don't know | 74 | 12 | | |
| *P*-value | | | | | |
| History of NMSC | None | 2449 | 187 | 1.00 | 1.00 |
| | Yes | 1081 | 86 | 0.91 (0.69, 1.20) | 0.93 (0.70, 1.23) |
| | Don't know | 48 | 2 | | |
| *P*-value | | | | 0.51 | 0.59 |

** Adjusted for center, primary status, crossover time-dependent status, age at diagnosis and sex.

+ Adjusted for center, primary status, crossover time-dependent status, age at diagnosis, sex, anatomic site, and education.

**Table 2**

Recent sun exposure and its association with melanoma survival.

| Variable | Level | No. in Study | No. Died from Melanoma | Baseline Model** HR (95% CI) | Fully Adjusted Model + HR (95% CI) |
|---|---|---|---|---|---|
| Sunburns within 10 years of diagnosis | 0 | 3246 | 240 | 1.00 | 1.00 |
| | 1+ | 252 | 4 | 0.36 (0.13, 0.98) | 0.27 (0.09, 0.85) |
| | Missing | 80 | 11 | | |
| *P*-value | | | | 0.05 | 0.03 |
| Holiday Sun Hours within 10 years of diagnosis | 0 | 1852 | 145 | 1.00 | 1.00 |
| | > 0 –<56.5 | 740 | 37 | 0.75 (0.52, 1.08) | 0.77 (0.53, 1.11) |
| | 56.5+ | 739 | 55 | 0.87 (0.63, 1.21) | 0.90 (0.65, 1.25) |
| | Missing | 247 | 18 | | |
| *P* for trend | | | | 0.28 | 0.38 |
| Water-related activities | 0<1314 | 848 | 60 | 1.00 | 1.00 |
| Within 10 years of diagnosis | 1314<3120 | 830 | 55 | 0.89 (0.61, 1.28) | 0.86 (0.59, 1.26) |
| | 3120<6140 | 868 | 63 | 0.87 (0.60, 1.25) | 0.87 (0.60, 1.26) |
| | 6140+ | 848 | 64 | 0.88 (0.61, 1.27) | 0.84 (0.48, 1.22) |
| | Missing | 183 | 13 | | |
| *P* for trend | | | | 0.51 | 0.41 |
| UVB dose | 0<2,134 kJ/m2 | 836 | 58 | 1.00 | 1.00 |
| Within 10 years of diagnosis | 2,134<3,757 kJ/m2 | 838 | 45 | 0.70 (0.47, 1.05) | 0.68 (0.46, 1.01) |
| | 3,757<6.413 kJ/m2 | 837 | 67 | 0.95 (0.66, 1.37) | 0.86 (0.59, 1.24) |
| | 6,413+ kJ/m2 | 837 | 69 | 0.78 (0.53, 1.15) | 0.69 (0.47, 1.02) |
| | Missing | | | | |
| *P* for trend | | | | 0.51 | 0.18 |
| Season of diagnosis | Winter | 741 | 52 | 1.00 | 1.00 |
| | Fall | 962 | 71 | 0.82 (0.64, 1.04) | 0.90 (0.62, 1.30) |
| | Spring | 803 | 50 | 0.87 (0.69, 1.11) | 0.97 (0.65, 1.45) |
| | Summer | 1060 | 81 | 0.89 (0.79, 1.16) | 1.09 (0.77, 1.55) |
| *P* for trend | | | | 0.49 | 0.46 |

** Adjusted for center, primary status, crossover time-dependent status, age at diagnosis and sex.

[+] Adjusted for center, primary status, crossover time-dependent status, age at diagnosis, sex, education and anatomic site.

**Table 3**

Early life sun exposure and its association with melanoma survival.

| Variable | Level | Number in Study | Number Dead from Melanoma | Baseline Model HR (95% CI)** | Fully Adjusted Model HR (95% CI)+ |
|---|---|---|---|---|---|
| Sunburns - Early life | 0 | 1584 | 114 | 1.00 | 1.00 |
| | 1+ | 1496 | 104 | 1.03 (0.78, 1.36) | 1.08 (0.81, 1.42) |
| | Missing | 498 | 37 | | |
| *P*-value | | | | 0.82 | 0.61 |
| Holiday Sun Hours -Early life | 0 | 2726 | 197 | 1.00 | 1.00 |
| | 1+ | 769 | 52 | 1.10 (0.80, 1.52) | 1.19 (0.86, 1.67) |
| | Missing | 83 | 6 | | |
| *P* -value | | | | 0.56 | 0.29 |
| Water related activities – early life | 0–<386 | 849 | 57 | 1.00 | 1.00 |
| | 386–<1404 | 848 | 57 | 1.02 (0.70, 1.49) | 1.02 (0.70, 1.49) |
| | 1404–<3414 | 852 | 57 | 0.96 (0.66, 1.41) | 0.91 (0.61, 1.35) |
| | 3414+ | 850 | 71 | 1.18 (0.82, 1.70) | 1.17 (0.81, 1.70) |
| | Missing | 179 | 13 | | |
| *P* for trend | | | | 0.42 | 0.49 |
| UVB dose - early life kJ/m$^2$ | 0–<3333 | 839 | 47 | 1.00 | 1.00 |
| | 3333–<4916.5 | 838 | 43 | 0.98 (0.64, 1.50) | 0.93 (0.60, 1.43) |
| | 4916.5–<6796 | 838 | 69 | 1.46 (0.97, 2.20) | 1.35 (0.89, 2.05) |
| | 6796+ | 839 | 77 | 1.65 (1.07, 2.52) | 1.49 (0.97, 2.31) |
| | Missing | 224 | 19 | | |
| *P* for trend | | | | 0.009 | 0.03 |

** Adjusted for center, primary status, crossover time-dependent status, age at diagnosis and sex.

+ Adjusted for center, primary status, crossover time-dependent status, age at diagnosis, sex, anatomic site,

**Table 4**

Average annual sun exposure in relationship to melanoma survival.

| Variable | Level | Number in Study | Number Melanoma Deaths | Baseline Model HR (95% CI)** | Fully Adjusted Model HR (95% CI)+ |
|---|---|---|---|---|---|
| Solar Elastosis | | | | | |
| | Absent | 889 | 55 | 1.00 | 1.00 |
| | Present | 1892 | 141 | 0.88 (0.63, 1.24) | 0.74 (0.51, 1.06) |
| | Missing | 797 | 59 | | |
| *P*-value | | | | 0.47 | 0.10 |
| Ever sunburned | No | 1139 | 86 | 1.00 | 1.00 |
| | Yes | 2174 | 167 | 1.05 (0.80, 1.36) | 1.05 (0.80, 1.37) |
| | Missing | 12 | 2 | | |
| *P*-value | | | | 0.75 | 0.75 |
| Holiday Sun Hours Average Annual | | | | | |
| | 0–<1.02 | 716 | 54 | 1.00 | 1.00 |
| | 1.02–<19.7 | 718 | 40 | 0.71 (0.47, 1.07) | 0.76 (0.50, 1.14) |
| | 19.7–<44.9 | 717 | 51 | 0.85 (0.58, 1.25) | 0.88 (0.59, 1.30) |
| | 44.9+ | 717 | 53 | 0.83 (0.56, 1.23) | 0.88 (0.59, 1.31) |
| | missing | 710 | 57 | | |
| *P* for trend | | | | 0.52 | 0.67 |
| Water-related activities - Average Annual | | | | | |
| | 0–<0.8 | 886 | 58 | 1.00 | 1.00 |
| | >0.8–<25.39 | 887 | 72 | 1.16 (0.81, 1.65) | 1.23 (0.86, 1.77) |
| | 25.39–<76.5 | 887 | 66 | 1.15 (0.80, 1.65) | 1.25 (0.86, 1.81) |
| | 76.5+ | 887 | 57 | 1.00 (0.69, 1.45) | 1.08 (0.74, 1.58) |
| | Missing | 31 | 2 | | |
| *P* for trend | | | | 0.95 | 0.72 |
| Average Annual UVB dose | | | | | |
| | 0–<2857 | 822 | 52 | 1.00 | 1.00 |
| *(kJ/m2)* | 2857–<4106.8 | 823 | 43 | 0.85 (0.55, 1.31) | 0.79 (0.51, 1.22) |

| Variable | Level | Number in Study | Number Melanoma Deaths | Baseline Model HR (95% CI)** | Fully Adjusted Model HR (95% CI)+ |
|---|---|---|---|---|---|
| | 4106.8–<5888 | 823 | 57 | 1.08 (0.71, 1.65) | 0.95 (0.62, 1.45) |
| | 5888+ | 823 | 80 | 1.23 (0.80, 1.89) | 1.10 (0.71, 1.70) |
| | Missing | 287 | 23 | | |
| *P* for trend | | | | 0.16 | 0.39 |

** Adjusted for center, primary status, crossover time-dependent status, age at diagnosis and sex.

+ Adjusted for center, primary status, crossover time-dependent status, age at diagnosis, sex, anatomic site, and education.



*Cancer Epidemiol Biomarkers Prev*. Author manuscript; available in PMC 2015 October 01.