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Indoor tanning and risk of early-onset basal cell carcinoma

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Abstract

Background—Despite a rise in incidence of basal cell carcinoma (BCC) among young people and the ubiquity of indoor tanning in this population, few epidemiologic studies have investigated this exposure-disease relationship.

Objective—Evaluate the association between indoor tanning and early-onset BCC.

Methods—BCC cases (n=376) and controls with minor benign skin conditions (n=390) under age 40 were identified through Yale Dermatopathology. Participants provided information on ever indoor tanning, age of initiation, frequency, duration, burns while tanning, and type of tanning device during an in-person interview. We calculated odds ratios (OR) and 95% confidence intervals (CI) using multivariate logistic regression with never indoor tanners as the referent group.

Results—Ever indoor tanning was associated with a 69% increased risk of early-onset BCC (95% CI=1.15-2.48). This association was stronger among women (OR=2.14, 95% CI=1.31-3.47), for multiple BCCs (OR=2.16, 95% CI=1.26-3.70), and for BCCs on the trunk and extremities (OR=2.81, 95% CI=1.57-5.02). Risk increased dose-dependently with years used regular indoor tanning devices (p-trend=0.003), number of overall burns (p-trend=<0.001) and burns to biopsy site (p-trend=<0.001) from indoor tanning. Approximately one-quarter (27%) of early-onset BCCs (or 43% among women) could be prevented if individuals never tanned indoors.

Limitations—Potential recall bias of indoor tanning by cases and generalizability of the control population suggest replication in other studies is warranted.

Conclusions—Indoor tanning was a strong risk factor for early-onset BCC, particularly among women. Indoor tanning should continue to be targeted by both policy-based and behavioral interventions, as the impact on BCC-associated morbidity may be substantial.

Keywords

basal cell carcinoma; epidemiology; indoor tanning; case-control; skin cancer; risk factors

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Introduction

In recent decades, the incidence of basal cell carcinoma (BCC), which comprises 80% of nonmelanoma skin cancers (NMSC),[1-2] has been increasing.[3-11] The rise has been striking among people under the age of 40,[3, 9, 12] especially women,[9, 12] pointing toward a corresponding change in environmental or lifestyle exposures. Because ultraviolet (UV) radiation is the primary environmental etiologic factor for BCC (reviewed in[13-15]), a logical hypothesis for the emergence of this malignancy among young people is increased exposure to UV.

Parallel trends of growing exposure to artificial UV from indoor tanning[16-17] and increases in BCC incidence provide support at the ecologic level for the hypothesis that indoor tanning is leading to increases in BCC incidence rates among young people. Prevalence estimates of indoor tanning in developed countries vary widely (2.8%-47.0% tanned indoors in prior year).[18] An estimated 30 million people tan indoors each year in the United States.[16] Young women are the individuals most likely to engage in this behavior,[18-19] lending additional support to indoor tanning playing a role in the changing patterns of BCC.

The International Agency for Research on Cancer (IARC) recently concluded there was "convincing evidence to support a causal association" between indoor tanning and melanoma and squamous cell skin cancer, but limited data for BCC did not support an association.[17] Thus far, only one population-based case-control study of non-melanoma skin cancer has observed a significant 50% increased risk of BCC with ever indoor tanning;[20] however, other research has been in populations of primarily older individuals with a low prevalence of indoor tanning.[21-25] There is new interest in early-onset BCC with intriguing findings for indoor tanning as a risk factor, but this research has been limited by small sample sizes.[26-27]

Because the relationship between indoor tanning and BCC has been inconsistent and markedly understudied in relation to early-onset BCC, we evaluated this association in a large case-control study of individuals under age 40 in which indoor tanning was quite prevalent. In the context of the rising incidence of BCC among young people and indoor tanning being a modifiable risk factor, better understanding the relationship between this exposure and BCC could have a considerable impact on primary prevention.

Materials and Methods

Yale Study of Skin Health in Young People

The Yale Study of Skin Health in Young People is a case-control study of early-onset BCC conducted in Connecticut (July 2007-December 2010) described in detail elsewhere.[28] BCC cases and controls with minor benign skin conditions diagnosed between July 1, 2006 and September 30, 2010 were identified through Yale University's Dermatopathology database. Eligible participants had to: be less than 40 years of age at the time of skin biopsy, reside in Connecticut, speak English, and themselves (or appropriate guardian for decisionally impaired individuals and those under age 18) be mentally and physically capable of completing all study components. Participants completed a structured in-person interview, self-administered questionnaires, and provided a saliva sample with Oragene®•DNA 2mL saliva collection kits (DNA Genotek Inc.; Ontario, Canada; http://www.dnagenotek.com/index.html). Yale University's Institutional Review Board approved the study (Protocol #0612002107, Approved: 02/02/2007) and study participants (or guardians) provided written informed consent.

Among the 665 potentially eligible BCC cases identified, 17 (2.6%) were ineligible upon initial contact: 14 lived out of state and 3 could not complete all study components. Of the remaining 648 individuals, 114 (17.6%) could not be contacted directly (no telephone number, non-working telephone number, only spoke to other person in household, left message only). Among the 534 cases we were able to directly reach and determine full eligibility, 389 enrolled (participation rate=72.8%) and 145 (27.2%) declined to participate. Cases were classified into single (only one BCC, n=242) or multiple (two or more BCCs, n=147) BCC under the age of 40 based on the Yale Dermatopathology database (data from 1990 on) and participant self-report.

Randomly sampled controls were frequency matched to BCC cases on age at biopsy (5 year age groups), gender, and biopsy site (head/neck, trunk, extremity). A variety of diagnoses were determined ineligible for sampling, including skin cancers/precancers (e.g., melanoma, squamous cell carcinoma, T-cell lymphomas, actinic keratoses), potentially UV-related benign conditions (e.g., solar lentigo, abnormal nevus), erythematous conditions associated with photosensitivity or aggravated by UV exposure (e.g. lupus erythematous, erythema multiforme, rosacea), dermal conditions treated with UV therapy (e.g., psoriasis), and pigment disorders (e.g., vitiligo). Among the 1,102 potentially eligible controls, 60 (5.4%) were ineligible upon initial contact (39 lived out of state, 10 non-English speakers, 2 did not recall having a skin biopsy, 1 hearing impaired, 1 hospitalized) or during the interview (7 self-reported a BCC). Of the remaining 1,042 individuals, 288 (27.6%) could not be contacted. Among the 754 potential controls we directly reached and determined full eligibility, 458 controls enrolled in the study (participation rate=60.7%) and 296 (39.3%) declined to participate. Our dermatologist (DJL) reviewed the individual diagnoses of all enrolled controls to ensure eligibility criteria were met. The most common control conditions were cyst (16.4%), seborrheic keratosis (16.2%), and wart (11.4%). All other conditions were present among less than 10% of controls.

Data Collection

The structured interview contained questions on sociodemographics, outdoor UV exposure (incidental exposure, intentional sunbathing), history of sunburns, sunscreen use, melanoma and non-melanoma skin cancer among first degree relatives, height, weight, alcohol intake, smoking status, and self-reported phenotype characteristics (eye, skin, and hair color; skin reaction to strong sunlight for the first time in the summer for one hour without sunscreen; skin reaction after repeated and prolonged exposure to sunlight; freckles on face; moles on the back ≥ 5 mm). Occupational UV exposure was gathered with a self-administered questionnaire. Questionnaires were adapted from those used by other recent epidemiologic studies[20] to facilitate future data pooling. Interviewers were blinded to case-control status until the end of the interview, when participants were asked about their personal history of cancer.

Participants were also asked about their indoor tanning history (using established instruments) and were provided color photos of different types of tanning beds/booths as visual aids. We queried ever use of indoor tanning (regular tanning beds/booths, high speed/high intensity tanning beds/booths, high pressure tanning beds/booths), age first indoor tanned, and number of burns (any part of the body, skin biopsy site) from indoor tanning. Across four specified age periods (ages 11-15, 16-20, 21-30, and 31 plus), we obtained frequency of use and average length of tanning sessions. Participants were also asked the total number of years they had used each type of tanning bed/booth.

Melanocortin 1 Receptor Gene (MC1R) Sequencing and Variant Classification

DNA was isolated from the saliva samples based on the manufacturer's protocol and variants in *MC1R* were obtained via sequencing, with the full methodology described previously.[28] Sequencing was conducted at W. M. Keck Facility at Yale University using Applied Biosystems 3730 capillary instruments. Sequencing reactions utilized fluorescently-labeled dideoxynucleotides (Big Dye Terminators) and Taq FS DNA polymerase in a thermal cycling protocol. The sequence was analyzed using Sequencher 4.9 (Gene Codes Corporation) comparing the query sequence to the standard sequence with no variants in *MC1R* (NM_002386.3). *MC1R* variants were classified into synonymous and non-synonymous variants. All laboratory personnel were blinded to case-control status.

Statistical Analysis

Our sample was limited to non-Hispanic Whites; 380 (97.7%) cases and 390 (85.2%) controls. One participant missing indoor tanning data and an additional three BCC cases with Gorlin Syndrome, which predisposes individuals to multiple BCCs early in life,[29] were further excluded, leaving an analytic population of 376 cases and 390 controls.

Using multivariate logistic regression, we calculated odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between indoor tanning and early-onset BCC. Continuous variables were categorized into tertiles based on the distribution of the exposures in controls who had tanned indoors; never indoor tanners served as the referent group. Our multivariate models included variables that altered the risk estimates by at least ten percent or were significantly associated with disease status in our population: skin color, family history of melanoma and/or non-melanoma skin cancer, first exposure of the season to one hour of summer sun, prolonged exposure to the sun, and *MC1R* non-synonymous variants. All models were also adjusted for the frequency matching variables of age at biopsy, body site of skin biopsy, and gender. Inclusion of the following exposures did not significantly alter risk estimates: education, eye color, hair color, moles ≥ 5 mm on back, freckles on face, body mass index (BMI), regular use of sunscreen, alcohol consumption, smoking status, incidental outdoor sun exposure, outdoor activities, sunburns, sunbathing sessions, and outdoor employment.

Trend tests were based on ordinal categorical variables representing the referent (never indoor tanners) and the tertiles of each exposure. We evaluated the linear trend using variables scored as the median of the tertiles, but due to the skewed nature of the exposures (e.g., tanning sessions, tanning hours), the ordinal scores appeared more appropriate and are presented here. This was supported by a goodness of fit test (χ^2 distribution with k-2 degrees of freedom) taking the difference between the χ^2 statistic from the model with k-1 variables for each exposure (where k=number of exposure categories) and 1) the χ^2 statistic for a model with the ordinal categorical variable; and 2) the χ^2 statistic for a model with the median scored variable.[30]

We tested interactions by body site of biopsy, skin color, *MC1R* variants, age at biopsy, and gender by including cross-product terms in the multivariate models. We calculated population attributable risk for case-control studies: P(E|D)(1-1/RR); where P=the proportion of cases exposed (E=exposure, D=disease) and RR=relative risk approximated by the OR based on the rare disease assumption.[30] All descriptive and multivariate analyses were conducted using SAS Version 9.2 (SAS, Cary, NC) and reported p-values, except for tests of trend, are two-sided.

Results

Of the 766 participants, 69.2% were female and the median age at skin biopsy was approximately 36 years. BCC cases were more likely to have fairer pigment-related characteristics, a family history of skin cancer, regularly used sunscreen on the body site of their skin biopsy, spent more time outdoors during warm months, and sunburned more frequently than controls (Table I). Cases were also more likely to have never smoked, have normal BMIs, and have attained higher education levels compared to controls.

Ever indoor tanning was associated with a 69% increased risk of early-onset BCC (OR=1.69, 95% CI=1.15-2.48) (Table II). This association was stronger for multiple BCC case status (OR=2.16, 95% CI=1.26-3.70) than single BCC cases (OR=1.46, 95% CI=0.96-2.22). In a sensitivity analysis removing controls with the three most common conditions one at a time, there was little impact on the association (data not shown).

Indoor tanning frequency was positively associated with early-onset BCC, with evidence for statistically significant increased risk across all three tertiles of sessions and the top two tertiles of hours spent indoor tanning (Table II). BCC risk was slightly higher for the youngest age of initiation (≤ 16 years OR=1.83, 95% CI=1.12-2.97) as compared to the upper tertiles. Dichotomizing at the median of 17.4 years elapsed between first indoor tanning and skin biopsy, we observed a slightly stronger association between indoor tanning and BCC with longer (OR=1.77, 95% CI=1.13-2.80) versus shorter (OR=1.63, 95% CI=1.07-2.51) time elapsed, although both were statistically significant.

Having been burned while indoor tanning (OR=1.87, 95% CI =1.17-2.97), particularly burning at the site of the skin biopsy (OR=2.72, 95% CI =1.57-4.69), was strongly associated with early-onset BCC (Table II). The number of overall burns (p-trend=<0.001) and number of burns specifically to the biopsy site (p-trend=<0.001) also showed a positive linear relationship with BCC.

Risk of early-onset BCC was significantly increased with ever use of each type of tanning bed/booth, with stronger associations for high speed/high intensity and high pressure tanning devices (Table II). Years of use of regular tanning beds/booths showed a positive linear relationship with BCC risk (p-trend=0.003), with those who tanned indoors six or more years greater than two-fold more likely to have BCC than never indoor tanners (OR=2.16, 95% CI=1.34-3.48). Years of use of high speed/high intensity (p-trend=0.030) and high pressure (p-trend=0.004) tanning beds/booths were also positively linearly associated with BCC (data not shown).

Females who tanned indoors were approximately two times more likely to have a BCC compared to female never indoor tanners (OR=2.14, 95% CI=1.31-3.47), whereas among men this association did not reach statistical significance (OR=1.16, 95% CI=0.60-2.25) (Table III). There was little evidence of an association between indoor tanning and BCCs located on the head/neck, yet there was an approximately two-fold and four-fold increased risk for BCCs on the trunk and extremities, respectively. When trunk and extremities were combined, body site significantly modified the effect of ever indoor tanning ($p_{interaction}$=0.012; OR=2.81, 95% CI=1.57-5.02). We observed stronger associations for ever indoor tanning among women by body site; non-significant 35% increased risk for BCC on the head/neck (95% CI=0.69-2.64) and statistically significant associations for BCC on the extremities (OR=6.55, 95% CI=1.87-22.95) and trunk (OR=2.89, 95% CI=1.08-7.65).

The adverse effect of indoor tanning was primarily observed in persons with one or more non-synonymous *MC1R* variants (OR=1.99, 95% CI=1.28-3.09), although the gene-environment interaction was not significant ($p_{interaction}$=0.194) (Table III). Indoor tanning

also appeared to be more harmful in persons who had very fair skin (OR=2.26, 95% CI=1.08-4.74), as compared to fair or olive skin (OR 1.56, 95% CI=0.99-2.46), but this interaction was also not significant ($p_{interaction}$=0.730). The association between indoor tanning and BCC was not modified by age at biopsy (data not shown).

Based on calculations of population attributable risk, approximately 27% of early-onset BCC cases could be prevented if individuals never tanned indoors. Among women under age 40, the proportion of preventable cases was even higher, with 43% of BCCs avoided if females did not tan indoors.

Discussion

In this case-control study of early-onset BCC, we observed a 69% increased risk of disease with ever indoor tanning. The indoor tanning association was stronger for cases with multiple BCCs and more pronounced for women, as female indoor tanners were two times more likely to have BCC than women who had never tanned indoors. Indoor tanning was also more strongly associated with BCCs located on the trunk and extremities, body sites likely to be exposed predominantly when tanning, as compared to lesions on the head/neck, which receive considerable incidental UV exposure.

Prior to this investigation, research on indoor tanning and BCC (summarized in Table IV) had largely been in older populations,[20-25] with only two small studies of early-onset BCC.[26-27] The prevalence of indoor tanning in studies of BCC cases of all ages has been quite low, and in combination with limited sample sizes, may have hindered the ability to detect associations if they existed. Several other studies, also with limited power and lack of quantitative measures, have evaluated indoor tanning in relation to multiple skin cancer types combined, with a 24% non-significant increased risk for skin malignancies on the head/neck[31] and null results for NMSCs in two hospital case-control studies.[32-33]

The summary association between indoor tanning and melanoma from a meta-analysis was statistically significant, but of fairly modest effect size (OR= 1.15, 95% CI=1.00-1.31).[17] However, much of the melanoma literature and many studies of indoor tanning and nonmelanoma skin cancer suffer from important limitations, including lack of sun exposure data, low prevalence of indoor tanning, and no quantitative information to examine dose-response relationships. Recent studies in melanoma, done in younger and more highly exposed populations, that addressed many of these limitations observed much stronger associations of melanoma with ever indoor tanning, as well as dose-response relationships.[34-35] In our study among a highly exposed population with extensive data on indoor tanning and sun exposure, the risk estimate for indoor tanning in relation to BCC was very similar to newer findings for melanoma,[34-35] highlighting the importance of study design and population exposure in interpreting findings regarding health effects of indoor tanning.

Age at initiation of indoor tanning may be an important component of skin cancer risk, as younger age at initiation has been more strongly associated with both melanoma overall[17] and early-onset melanoma,[35] with a suggestive trend for BCC.[20] However, other evidence suggests a similar melanoma risk regardless of the age at initiation.[34] The latter observation is consistent with our findings of increased risk of early-onset BCC across all ages of initiation of indoor tanning, but the range of age of when individuals first tanned indoors was fairly narrow in our young population; 95% started tanning indoors when they were 25 years of age or less and half reported their first use at age 17 or under.

In our sample, indoor tanning was much more common and frequent among women, and our population being predominantly female, limited our ability to examine the association in

males. The stronger effect of indoor tanning in women is likely due to a number of factors, including earlier age at initiation, greater number of tanning sessions (more individuals with greater exposure), and a larger proportion of women with tumors located on the trunk and extremities, which were more strongly related to indoor tanning in our data. While exposure differences are the most likely explanation for the gender difference, some of the observed effects could be due to other unidentified factors and should be investigated in future larger or pooled studies. Of note, among men we saw the same pattern by body site, with elevated, though non-significant, associations for indoor tanning in relation to trunk and extremity BCCs. The differences we observed by body site are important, as they highlight that for those body parts that are less likely to be exposed to incidental solar UV, the effect of indoor tanning may be more pronounced. Consideration of body site in future studies may be necessary to accurately characterize risk. Our finding of an increased risk of UV from indoor tanning on BCC among individuals with at least one non-synonymous variant in *MC1R* suggests potential interactions between this gene and UV exposure that should be explored in larger studies.

Burns from indoor tanning were strongly related to risk of early-onset BCC; with evidence of a dose-response effect. Potential recall bias could be particularly relevant to reporting burns specifically to the biopsy site. Conversely, social desirability bias may have also been an issue, with BCC cases possibly under-reporting overall indoor tanning. Although the impact of these potential biases on our results are unknown, the percentage of cases and controls, 28% and 23% respectively, who reported burns from indoor tanning, was similar to the approximately 20% of individuals in general population samples who reported burns from tanning indoors in the previous 12 months.[36-38]

Our study had several important strengths including adequate power, particularly among women, to examine the relationship between BCC and indoor tanning in an extremely relevant population, as well as assessment of numerous exposures as potential confounders. We were also able to evaluate dose-response relationships and as these were statistically significant, lend strength to our findings. Our study design limited the potential for interviewer bias, and because controls had also undergone skin biopsy, the potential for differential recall of behaviors by case status may have been minimized. In addition, by identifying cases and controls from a centralized dermatopathology facility serving many dermatologists in Connecticut, our controls represent the source population of our cases; that is, young people who see a dermatologist for a skin condition. Because study participants were all under age 40 at the time of skin biopsy, their reporting of indoor tanning was less subject to poor recall than older populations. Our sensitivity analyses removing individual control diagnoses indicated our findings were not driven by the inclusion of any particular benign condition.

In addition to the potential biases mentioned earlier, as in any observational study, it is possible that the association we observed is due, in part, to other unmeasured factors or residual confounding. Arguing against this, we considered known correlates of indoor tanning[18] and evaluated numerous characteristics as potential confounders, including incidental and intentional sun exposure. In addition, there is a chance that participants in our study were not representative of all individuals under age 40 in Connecticut seen by dermatologists. Another limitation is related to our control group being individuals who saw a dermatologist for biopsy of a benign skin condition and the potential for their indoor tanning behaviors to differ from a more general population sample of people under age 40. Our controls may be very aware of their skin health and therefore less likely to tan indoors than the general population. Alternatively, our control group may be enriched with individuals highly focused on their appearance who utilize indoor tanning to a greater extent. While population-based controls are often sought in case-control studies, because our

cases either sought out or were referred for dermatologic evaluation for a lesion under age 40, which could track with factors like socioeconomic status or insurance status that may also be correlated with tanning, population-based controls could also have introduced bias.

Indoor tanning was a strong risk factor for BCC in a population of individuals under age 40. We observed stronger associations in women, for BCCs located on the trunk and extremities, and for multiple BCCs. With a lack of epidemiologic data on indoor tanning and BCC risk in any age group, this research adds substantially to our understanding of this relationship. Our findings are in line with and extend the recent conclusions of IARC classifying UV-emitting tanning devices as Group I carcinogens.[39] While additional replication in studies with different control populations and/or in studies with prospectively collected exposure data on indoor tanning are necessary to confirm the positive association we observed between indoor tanning and BCC, our results fulfill many of the criteria for causality including biologic plausibility, strength of the association, dose-response effects, specificity of effect to the body sites most uniquely exposed to indoor tanning, and coherent findings with melanoma studies. The increased prevalence of indoor tanning, especially in young women, parallels an increase in BCC, which is also more pronounced in young women. We thus conclude that indoor tanning is a risk factor for early-onset BCC and appears to be causally contributing to the increasing incidence of this malignancy. Both policy-based and behavioral interventions, to restrict or reduce indoor tanning in young people, are needed to alter the increasing incidence of this most common human malignancy.

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Abbreviations

BCC	basal cell carcinoma
BMI	body mass index
CI	confidence interval
IARC	International Agency for Research on Cancer
MC1R	Melanocortin 1 Receptor Gene
NMSC	non-melanoma skin cancer
OR	odds ratio
UV	ultraviolet

References

1. Rogers HW, Weinstock MA, Harris AR, Hinckley MR, Feldman SR, Fleischer AB, et al. Incidence estimate of nonmelanoma skin cancer in the United States, 2006. Arch Dermatol. 2010; 146:283–7. [PubMed: 20231499]
2. American Cancer Society Skin Cancer. [May 2011] Basal and Squamous Cell. http://www.cancer.org/cancer/skincancer-basalandsquamouscell/detailedguide/skin-cancer-basal-and-squamous-cell-what-is-basal-and-squamous-cell.
3. Bath-Hextall F, Leonardi-Bee J, Smith C, Meal A, Hubbard R. Trends in incidence of skin basal cell carcinoma. Additional evidence from a UK primary care database study. Int J Cancer. 2007; 121:2105–8. [PubMed: 17640064]
4. Hughes JR, Higgins EM, Smith J, Du Vivier AW. Increase in non-melanoma skin cancer--the King's College Hospital experience (1970-92). Clinical & Experimental Dermatology. 1995; 20:304–7. [PubMed: 8548987]
5. Levi F, Te VC, Randimbison L, Erler G, La Vecchia C. Trends in skin cancer incidence in Vaud: an update, 1976-1998. Eur J Cancer Prev. 2001; 10:371–3. [PubMed: 11535880]
6. Karagas MR, Greenberg ER, Spencer SK, Stukel TA, Mott LA. Increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA. New Hampshire Skin Cancer Study Group. Int J Cancer. 1999; 81:555–9. [PubMed: 10225444]
7. Flohil SC, de Vries E, Neumann HA, Coebergh JW, Nijsten T. Incidence, prevalence and future trends of primary basal cell carcinoma in the Netherlands. Acta Derm Venereol. 2011; 91:24–30. [PubMed: 21264452]
8. Hannuksela-Svahn A, Pukkala E, Karvonen J. Basal cell skin carcinoma and other nonmelanoma skin cancers in Finland from 1956 through 1995. Arch Dermatol. 1999; 135:781–6. [PubMed: 10411152]
9. Birch-Johansen F, Jensen A, Mortensen L, Olesen AB, Kjaer SK. Trends in the incidence of nonmelanoma skin cancer in Denmark 1978-2007: Rapid incidence increase among young Danish women. Int J Cancer. 2010; 127:2190–8. [PubMed: 20473901]
10. Doherty VR, Brewster DH, Jensen S, Gorman D. Trends in skin cancer incidence by socioeconomic position in Scotland, 1978-2004. Br J Cancer. 2010; 102:1661–4. [PubMed: 20442712]
11. Arits AH, Schlangen MH, Nelemans PJ, Kelleners-Smeets NW. Trends in the incidence of basal cell carcinoma by histopathological subtype. J Eur Acad Dermatol Venereol. 25:565–9. [PubMed: 20840348]
12. Christenson LJ, Borrowman TA, Vachon CM, Tollefson MM, Otley CC, Weaver AL, et al. Incidence of basal cell and squamous cell carcinomas in a population younger than 40 years. JAMA. 2005; 294:681–90. [PubMed: 16091570]
13. Dessinioti C, Antoniou C, Katsambas A, Stratigos AJ. Basal cell carcinoma: what's new under the sun. Photochem Photobiol. 2010; 86:481–91. [PubMed: 20550646]
14. Madan V, Hoban P, Strange RC, Fryer AA, Lear JT. Genetics and risk factors for basal cell carcinoma. Br J Dermatol. 2006; 154(Suppl 1):5–7. [PubMed: 16712709]
15. Madan V, Lear JT, Szeimies RM. Non-melanoma skin cancer. Lancet. 2010; 375:673–85. [PubMed: 20171403]
16. Levine JA, Sorace M, Spencer J, Siegel DM. The indoor UV tanning industry: a review of skin cancer risk, health benefit claims, and regulation. J Am Acad Dermatol. 2005; 53:1038–44. [PubMed: 16310065]
17. International Agency for Research on Cancer Working Group on artificial ultraviolet (UV) light and skin cancer. The association of use of sunbeds with cutaneous malignant melanoma and other skin cancers: A systematic review. Int J Cancer. 2007; 120:1116–22. [PubMed: 17131335]
18. Coups EJ, Phillips LA. A more systematic review of correlates of indoor tanning. J Eur Acad Dermatol Venereol. 2011; 25:610–6. author reply 7-8. [PubMed: 21349117]
19. Schneider S, Kramer H. Who uses sunbeds? A systematic literature review of risk groups in developed countries. J Eur Acad Dermatol Venereol. 2009; 24:639–48. [PubMed: 20015180]

20. Karagas MR, Stannard VA, Mott LA, Slattery MJ, Spencer SK, Weinstock MA. Use of tanning devices and risk of basal cell and squamous cell skin cancers. J Natl Cancer Inst. 2002; 94:224–6. [PubMed: 11830612]
21. Walther U, Kron M, Sander S, Sebastian G, Sander R, Peter RU, et al. Risk and protective factors for sporadic basal cell carcinoma: results of a two-centre case-control study in southern Germany. Clinical actinic elastosis may be a protective factor. Br J Dermatol. 2004; 151:170–8. [PubMed: 15270887]
22. Bajdik CD, Gallagher RP, Astrakianakis G, Hill GB, Fincham S, McLean DI. Non-solar ultraviolet radiation and the risk of basal and squamous cell skin cancer. Br J Cancer. 1996; 73:1612–4. [PubMed: 8664139]
23. Corona R, Dogliotti E, D'Errico M, Sera F, Iavarone I, Baliva G, et al. Risk factors for basal cell carcinoma in a Mediterranean population: role of recreational sun exposure early in life. Arch Dermatol. 2001; 137:1162–8. [PubMed: 11559211]
24. Han J, Colditz GA, Hunter DJ. Risk factors for skin cancers: a nested case-control study within the Nurses' Health Study. Int J Epidemiol. 2006; 35:1514–21. [PubMed: 16943234]
25. Rosso S, Joris F, Zanetti R. Risk of basal and squamous cell carcinomas of the skin in Sion, Switzerland: a case-control study. Tumori. 1999; 85:435–42. [PubMed: 10774562]
26. Bakos RM, Kriz M, Muhlstadt M, Kunte C, Ruzicka T, Berking C. Risk factors for early-onset basal cell carcinoma in a German institution. Eur J Dermatol. 2011; 21(5):705–9. [PubMed: 21697066]
27. Boyd AS, Shyr Y, King LE Jr. Basal cell carcinoma in young women: an evaluation of the association of tanning bed use and smoking. J Am Acad Dermatol. 2002; 46:706–9. [PubMed: 12004311]
28. Ferrucci LM, Cartmel B, Molinaro AM, Gordon PB, Leffell DJ, Bale AE, et al. Host phenotype characteristics and MC1R in relation to early-onset basal cell carcinoma. J Invest Dermatol. In Press.
29. Gorlin RJ, Goltz RW. Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib. A syndrome. N Engl J Med. 1960; 262:908–12. [PubMed: 13851319]
30. Jewell, N. Statistics in Epidemiology. Chapman & Hall/CRC; Boca Raton, FL: 2004.
31. Hogan DJ, To T, Wilson ER, Miller AB, Robson D, Holfeld K, et al. A study of acne treatments as risk factors for skin cancer of the head and neck. Br J Dermatol. 1991; 125:343–8. [PubMed: 1835402]
32. Herity B, O'Loughlin G, Moriarty MJ, Conroy R. Risk factors for non-melanoma skin cancer. Ir Med J. 1989; 82:151–2. [PubMed: 2621075]
33. O'Loughlin C, Moriarty MJ, Herity B, Daly L. A re-appraisal of risk factors for skin carcinoma in Ireland. A case control study. Ir J Med Sci. 1985; 154:61–5. [PubMed: 3988489]
34. Lazovich D, Vogel RI, Berwick M, Weinstock MA, Anderson KE, Warshaw EM. Indoor tanning and risk of melanoma: a case-control study in a highly exposed population. Cancer Epidemiol Biomarkers Prev. 2010; 19:1557–68. [PubMed: 20507845]
35. Cust AE, Armstrong BK, Goumas C, Jenkins MA, Schmid H, Hopper JL, et al. Sunbed use during adolescence and early adulthood is associated with increased risk of early-onset melanoma. Int J Cancer. 2011; 128:2425–35. [PubMed: 20669232]
36. Rhainds M, De Guire L, Claveau J. A population-based survey on the use of artificial tanning devices in the Province of Quebec, Canada. J Am Acad Dermatol. 1999; 40:572–6. [PubMed: 10188676]
37. Boldeman C, Beitner H, Jansson B, Nilsson B, Ullen H. Sunbed use in relation to phenotype, erythema, sunscreen use and skin diseases. A questionnaire survey among Swedish adolescents. Br J Dermatol. 1996; 135:712–6. [PubMed: 8977669]
38. Boldeman C, Branstrom R, Dal H, Kristjansson S, Rodvall Y, Jansson B, et al. Tanning habits and sunburn in a Swedish population age 13-50 years. Eur J Cancer. 2001; 37:2441–8. [PubMed: 11720841]
39. El Ghissassi F, Baan R, Straif K, Grosse Y, Secretan B, Bouvard V, et al. A review of human carcinogens--part D: radiation. Lancet Oncol. 2009; 10:751–2. [PubMed: 19655431]

Table I

Selected characteristics among non-hispanic white BCC cases and controls in the Yale Study of Skin Health in Young People (N=766)

Characteristic	Cases, N=376 N[1] (%)	Controls, N=390 N[1] (%)	p-value[2]
Age (y), median (IQR)	36.3 (33.2-38.5)	36.8 (32.8-38.5)	0.923
Female	256 (68.1)	274 (70.3)	0.515
Body site of skin biopsy			<0.001
Head	204 (54.3)	164 (42.1)	
Extremity	72 (19.2)	126 (32.3)	
Trunk	100 (26.6)	100 (25.6)	
Education			0.012
≤ Some college	104 (27.7)	143 (36.9)	
College graduate	113 (30.1)	116 (29.9)	
≥ Some graduate school	158 (42.1)	129 (33.2)	
Eye color			<0.001
Brown	86 (22.9)	154 (39.5)	
Hazel	65 (17.3)	72 (18.5)	
Green	47 (12.5)	38 (9.7)	
Blue/Grey	178 (47.3)	126 (32.3)	
Hair color			<0.001
Black/Dark brown	101 (26.9)	161 (41.3)	
Light brown	135 (36.0)	155 (39.7)	
Blonde/Fair	100 (26.7)	63 (16.2)	
Red	39 (10.4)	11 (2.8)	
Skin color (inner upper arm)			<0.001
Olive	15 (4.0)	77 (19.7)	
Fair	212 (56.4)	236 (60.5)	
Very fair	149 (39.6)	77 (19.7)	
Skin reaction with first summer sun exposure			<0.001
Turn brown, no sunburn	6 (1.6)	31 (8.0)	
Mild sunburn followed by tan	142 (37.8)	200 (51.4)	
Painful sunburn peeling	198 (52.7)	144 (37.0)	
Severe sunburn blistering	30 (8.0)	14 (3.6)	
Skin reaction with prolonged sun exposure			<0.001
Very brown, deeply tanned	38 (10.1)	71 (18.2)	
Moderately tanned	169 (44.9)	223 (57.2)	
Mildly tanned peeling tendency	123 (32.7)	78 (20.0)	
Freckled, no suntan	46 (12.2)	18 (4.6)	
Moles ≥ 5 mm on back (n), median (IQR)	1 (0-3)	0 (0-2)	0.004
Freckles on face			<0.001
None	78 (20.7)	139 (35.6)	

Characteristic	Cases, N=376 N[1] (%)	Controls, N=390 N[1] (%)	p-value[2]
Very Few	81 (21.5)	112 (28.7)	
Few	123 (32.7)	93 (23.9)	
Some	74 (19.7)	36 (9.2)	
Many	20 (5.3)	10 (2.6)	
MC1R non-synonymous variants			<0.001
0 variants	65 (17.3)	131 (34.2)	
1 variant	173 (46.1)	175 (45.7)	
≥ 2 variants	137 (36.5)	77 (20.1)	
Family history of skin cancer	246 (65.4)	153 (29.2)	<0.001
Body mass index (kg/m^2)			<0.001
<25.0	246 (65.4)	209 (53.6)	
25-29.9	90 (23.9)	106 (27.2)	
≥ 30.0	40 (10.6)	75 (19.2)	
Regular use of sunscreen on biopsy site	76 (20.2)	43 (11.0)	<0.001
Ever drank alcohol ≥ once/week for ≥6 months	282 (76.2)	277 (71.9)	0.181
Smoking status			<0.001
Never	233 (62.5)	199 (51.4)	
Former	111 (29.8)	122 (31.5)	
Current	29 (7.8)	66 (17.1)	
Outdoor sun exposure in warm months (h), mean ± SD	8938 ± 3426	8310 ± 3265	0.010[3]
Outdoor activities (h), median (IQR)	6825 (3286-11397)	6260 (3204-11475)	0.431
Sunburns (n), median (IQR)	6 (1-16)	3 (1-9)	<0.001
Sunbathing sessions (n), median (IQR)	315 (58-713)	279 (84-689)	0.622
Employed in outdoor job (months), median (IQR)	0 (0-12)	0 (0-10)	0.265

[1] May not sum to total due to missing values.

[2] χ^2 for categorical variables, Wilcoxon Rank Sum for continuous variables.

[3] T-test

Table II

Odds ratios (OR) and 95% confidence intervals (CIs) for the association between indoor tanning and early-onset BCC in the Yale Study of Skin Health. For all variables the referent group is never indoor tanning.

Characteristic	Cases/Controls	Minimally Adjusted OR[1] (95% CI)	Cases/Controls	Multivariate OR[2] (95% CI)
Indoor tanning				
Never	129/141	1.00	129/137	1.00
Ever	247/249	1.21 (0.87-1.69)	246/245	1.69 (1.15-2.48)
Indoor tanning sessions (n)				
1-18	84/83	1.17 (0.78-1.75)	83/81	1.64 (1.04-2.59)
19-135	88/82	1.32 (0.87-2.00)	88/82	1.75 (1.09-2.82)
≥ 136	74/83	1.16 (0.75-1.79)	74/81	1.71 (1.04-2.81)
P-trend[3]		0.388		0.028
Indoor tanning hours				
>0-3.3	73/80	1.06 (0.70-1.61)	72/79	1.47 (0.92-2.35)
>3.3-29.2	96/85	1.40 (0.93-2.11)	96/84	1.89 (1.19-3.01)
>29.2	74/83	1.15 (0.74-1.77)	74/81	1.71 (1.04-2.82)
P-trend[3]		0.292		0.015
Age at initiation (y)				
≤ 16	93/97	1.23 (0.81-1.87)	93/96	1.83 (1.12-2.97)
>17-18	66/66	1.18 (0.76-1.85)	65/64	1.67 (1.01-2.76)
>18	88/85	1.23 (0.82-1.83)	88/84	1.64 (1.04-2.58)
Burned from indoor tanning				
No	143/159	1.11 (0.77-1.58)	142/155	1.61 (1.07-2.43)
Yes	104/89	1.44 (0.96-2.16)	104/89	1.87 (1.17-2.97)
Burns from indoor tanning (n)				
1	22/34	0.89 (0.47-1.67)	22/34	1.34 (0.64-2.81)
2-3	22/31	1.03 (0.54-1.97)	22/31	1.23 (0.58-2.60)
≥ 4	60/24	3.61 (2.01-6.47)	60/24	5.17 (2.56-10.47)
P-trend[3]		<0.001		<0.001
Biopsy site burned from indoor tanning				
No	173/207	1.03 (0.73-1.45)	172/203	1.48 (1.00-2.21)
Yes	73/40	2.31 (1.42-3.76)	73/40	2.72 (1.57-4.69)
Biopsy site burns from indoor tanning (n)				
1	16/16	1.58 (0.72-3.49)	16/16	2.05 (0.78-5.36)
2-3	19/11	2.56 (1.11-5.90)	19/11	3.83 (1.43-10.29)
≥ 4	39/13	4.95 (2.38-10.29)	39/13	6.90 (2.92-16.31)
P-trend[3]		<0.001		<0.001
Ever used device				
Regular tanning bed/booth	241/242	1.21 (0.86-1.68)	240/238	1.68 (1.14-2.46)
High speed/high intensity	95/100	1.45 (0.93-2.24)	95/99	2.26 (1.33-3.83)

Characteristic	Cases/Controls	Minimally Adjusted OR[1] (95% CI)	Cases/Controls	Multivariate OR[2] (95% CI)
High pressure	30/35	1.49 (0.80-2.75)	30/35	2.89 (1.34-6.24)
Years used regular tanning bed/booth				
1-2	77/84	1.07 (0.71-1.62)	76/84	1.49 (0.94-2.37)
3-5	63/70	1.05 (0.67-1.63)	63/68	1.46 (0.88-2.42)
6-26	101/87	1.54 (1.02-2.34)	101/85	2.16 (1.34-3.48)
P-trend[3]		0.057		0.003

[1]Adjusted for frequency matching study variables: age at diagnosis, body site, and gender.

[2]Adjusted for age at diagnosis (continuous), body site (head/neck, trunk, extremity), gender, skin color (olive, fair, very fair), family history of melanoma and/or non-melanoma skin cancer (yes, no), first exposure of the season to one hour of summer sun (turn brown with no sunburn, mild sunburn followed by some degree of tanning, painful sunburn for a few days followed by peeling, severe sunburn with blistering), prolonged exposure to the sun (very brown and deeply tanned, moderately tanned, only mildly tanned due to tendency to peel, only freckled or no suntan at all), and *MC1R* non-synonymous variants (0, 1, ≥2 variants).

[3]Based on ordinal categorical variables.

Table III

Odds ratios (OR) and 95% confidence intervals (CIs) for the association between indoor tanning and BCC in the Yale Study of Skin Health stratified by selected characteristics

Characteristic	Indoor Tanning	Cases/Controls	Multivariate OR[1] (95% CI)	p for interaction[2]
Gender				0.019
Male	Never	81/68	1.00	
	Ever	39/44	1.16 (0.60-2.25)	
Female	Never	48/69	1.00	
	Ever	207/201	2.14 (1.31-3.47)	
Body Site				0.056
Head/neck	Never	89/60	1.00	
	Ever	115/101	1.11 (0.66-1.86)	
Extremity (includes shoulder)	Never	17/45	1.00	
	Ever	55/80	3.94 (1.56-9.98)	
Trunk	Never	23/32	1.00	
	Ever	76/64	2.20 (1.01-4.81)	
***MC1R* non-synonymous variants**				0.194
0 variants	Never	25/45	1.00	
	Ever	40/85	1.09 (0.50-2.38)	
≥ 1 variants	Never	104/92	1.00	
	Ever	206/160	1.99 (1.28-3.09)	
Skin color				0.730
Olive/Fair	Never	63/101	1.00	
	Ever	163/205	1.56 (0.99-2.46)	
Very Fair	Never	66/36	1.00	
	Ever	83/40	2.26 (1.08-4.74)	

[1]Each strata adjusted for all other characteristics: age at diagnosis (continuous), body site (head/neck, trunk, extremity), skin color (olive, fair, very fair), family history of melanoma and/or non-melanoma skin cancer (yes, no), first exposure of the season to one hour of summer sun (turn brown with no sunburn, mild sunburn followed by some degree of tanning, painful sunburn for a few days followed by peeling, severe sunburn with blistering), prolonged exposure to the sun (very brown and deeply tanned, moderately tanned, only mildly tanned due to tendency to peel, only freckled or no suntan at all), and *MC1R* non-synonymous variants (0, 1, ≥2 variants).

[2]Based on inclusion of cross-product term in multivariate model.

Table IV

Summary of research on indoor tanning and/or sunlamps and risk of BCC.

Reference	Country	Population	Cases/Controls	Prevalence or measure of indoor tanning in cases	OR[1] (95% CI)
Early-onset BCC					
Bakos et al. (2011)	Germany	Men and women, age 19-40, hospital-based sample	25/25	Regular use of tanning beds=68%	25.0 (2.26-277.36)
Boyd et al. (2002)	US	Women age 20-40, one university dermatopathology division	30/30	Average number of indoor tanning sessions=152.2	OR not reported, p=0.35 for difference in mean number of sessions
Ferrucci et al. (2011)	US	Men and women, under age 40, university dermatopathology facility serving dermatologists in Connecticut	375/382	Ever indoor tanning=66%	1.69 (1.15-2.48)
Cases not selected for age at onset					
Bajdik et al. (1996)	Canada	Men age 25-79, population-based sample from Alberta	226/404	Ever use of sunlamps=10%	1.2 (0.7-2.2)
Corona et al. (2001)	Italy	Men and women, age range not listed, hospital-based sample	166/158	Ever use of sunbeds or sunlamps=11%	0.6 (0.3-1.2)
Han et al. (2006)	US	Women, age 43-68 at start of follow-up, nested case-control in Nurses' Health Study	259/712	Ever use of sunlamps or tanning salon=17%	1.32 (0.87-2.03)
Karagas et al. (2002)	US	Men and women, age 25-74, population-based sample	601/539	Ever indoor tanning=21%	1.5 (1.1-2.1)
Rosso et al. (1999)	Switzerland	Men and women, age 20-75, population bases sample from Sion	120/144	Ever use of sunlamps=8.3%	1.24 (0.53-2.88)
Walther et al. (2004)	Germany	Men and women, case median age 69, hospital-based sample	213/411	Use of artificial UV radiation or UV beds >5 times per year=4%	0.7 (0.3-1.5) Unadjusted for >5 vs <=5 times per year

[1] Multivariate, unless noted otherwise