

# Indoor tanning and risk of early-onset basal cell carcinoma

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**Background:** Despite an increase 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:** We sought to evaluate the association between indoor tanning and early-onset BCC.

**Methods:** Patients with BCC (n = 376) and control subjects with minor benign skin conditions (n = 390) who were younger than 40 years of age 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 females (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 using regular indoor tanning devices (*P* trend = .003), number of overall burns (*P* trend < .001), and burns to biopsy site (*P* trend < .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 patients 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 females. Indoor tanning should continue to be targeted by both policy-based and behavioral interventions, as the impact on BCC-associated morbidity may be substantial. (J Am Acad Dermatol 2012;67:552-62.)

**Key words:** basal cell carcinoma; case-control; epidemiology; indoor tanning; risk factors; skin cancer.

In recent decades, the incidence of basal cell carcinoma (BCC), which comprises 80% of nonmelanoma skin cancers (NMSC),<sup>1,2</sup> has been increasing.<sup>3-11</sup> The increase has been striking among people younger than 40 years,<sup>3,9,12</sup> especially women,<sup>9,12</sup> pointing toward a corresponding change in environmental or lifestyle exposures. Because ultraviolet (UV) radiation is the primary environmental causal factor for BCC,<sup>13-15</sup> a logical hypothesis for

## Abbreviations used:

BCC:	basal cell carcinoma
CI:	confidence interval
IARC:	International Agency for Research on Cancer
MC1R:	melanocortin 1 receptor gene
NMSC:	nonmelanoma skin cancer
OR:	odds ratio
UV:	ultraviolet

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the emergence of this malignancy among young people is increased exposure to UV.

Parallel trends of growing exposure to artificial UV from indoor tanning<sup>16,17</sup> 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).<sup>18</sup> An estimated 30 million people tan indoors each year in the United States.<sup>16</sup> Young women are the individuals most likely to engage in this behavior,<sup>18,19</sup> 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.<sup>17</sup> Thus far, only one population-based case-control study of NMSC has observed a significant 50% increased risk of BCC with ever indoor tanning<sup>20</sup>; however, other research has been in populations of primarily older individuals with a low prevalence of indoor tanning.<sup>21–25</sup> 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.<sup>26,27</sup>

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 younger than 40 years in which indoor tanning was quite prevalent. In the context of the increasing 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.

## 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.<sup>28</sup> Patients with BCC and control subjects with minor benign skin conditions given a diagnosis between July 1, 2006, and September 30, 2010, were identified through the Yale University Dermatopathology database. Eligible participants had to: be younger than 40 years at the time of skin biopsy, reside in Connecticut, speak English,

and themselves (or appropriate guardian for decisionally impaired individuals and those aged <18 years) be mentally and physically capable of completing all study components. Participants completed a structured in-person interview, completed self-administered questionnaires, and provided a saliva sample with Oragene DNA 2-mL saliva collection kits (DNA Genotek Inc, Ottawa, Ontario, Canada). Yale University Institutional Review Board approved the study (protocol number 0612002107; approved February 2, 2007) and study participants (or guardians)

provided written informed consent.

Among the 665 potentially eligible patients with BCC 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, nonworking telephone number, only spoke to other person in household, left message only). Among the 534 patients we were able to directly reach and determine full eligibility, 389 enrolled (participation rate = 72.8%) and 145 (27.2%) declined to participate. Patients were classified into single (only 1 BCC,  $n = 242$ ) or multiple ( $\geq 2$  BCCs,  $n = 147$ ) BCC aged younger than 40 years based on the Yale Dermatopathology database (data from  $\geq 1990$ ) and participant self-report.

Randomly sampled control subjects were frequency matched to patients with BCC 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 (eg, melanoma, squamous cell carcinoma, T-cell lymphomas, actinic keratoses), potentially UV-related benign conditions (eg, solar lentigo, abnormal nevus), erythematous conditions associated with photosensitivity or

## CAPSULE SUMMARY

- Indoor tanning has been associated with melanoma, but epidemiologic studies in relation to basal cell carcinoma are limited and inconsistent.
- Indoor tanning was associated with a 69% increased risk of early-onset basal cell carcinoma in this case-control study; among females the association was stronger.
- As previously shown for melanoma in younger persons, indoor tanning contributed substantially to basal cell carcinoma risk in young people, strengthening the need for interventions to restrict/reduce indoor tanning.

aggravated by UV exposure (eg, lupus erythematosus, erythema multiforme, rosacea), dermal conditions treated with UV therapy (eg, psoriasis), and pigment disorders (eg, vitiligo). Among the 1102 potentially eligible control subjects, 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 1042 individuals, 288 (27.6%) could not be contacted. Among the 754 potential control subjects we directly reached and determined full eligibility, 458 control subjects enrolled in the study (participation rate = 60.7%) and 296 (39.3%) declined to participate. Our dermatologist (D. J. L.) reviewed the individual diagnoses of all enrolled control subjects 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 control subjects.

### Data collection

The structured interview contained questions on sociodemographics, outdoor UV exposure (incidental exposure, intentional sunbathing), history of sunburns, sunscreen use, melanoma and NMSC 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 1 hour without sunscreen; skin reaction after repeated and prolonged exposure to sunlight; freckles on face; moles on the back  $\geq 5$  mm). Occupational UV exposure was gathered with a self-administered questionnaire. Questionnaires were adapted from those used by other recent epidemiologic studies<sup>20</sup> 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 photographs 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 4 specified age periods (11-15, 16-20, 21-30, and  $\geq 31$  years), 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 sequencing and variant classification

DNA was isolated from the saliva samples based on the manufacturer's protocol and variants in melanocortin 1 receptor gene (*MC1R*) were obtained via sequencing, with the full methodology described previously.<sup>28</sup> Sequencing was conducted at W. M. Keck Facility at Yale University using Applied Biosystems 3730 capillary instruments (Applied Biosystems, Carlsbad, CA). Sequencing reactions used fluorescently labeled dideoxynucleotides (Big Dye Terminators, Applied Biosystems) and Taq FS DNA polymerase in a thermal cycling protocol. The sequence was analyzed using Sequencher 4.9 (Gene Codes Corp, Ann Arbor, MI) comparing the query sequence with the standard sequence with no variants in *MC1R* (NM\_002386.3). *MC1R* variants were classified into synonymous and nonsynonymous variants. All laboratory personnel were blinded to case-control status.

### Statistical analysis

Our sample was limited to non-Hispanic whites: 380 (97.7%) BCC patients and 390 (85.2%) control subjects. One participant missing indoor tanning data and an additional 3 patients with BCC and Gorlin syndrome, which predisposes individuals to multiple BCCs early in life,<sup>29</sup> were further excluded, leaving an analytic population of 376 patients and 390 control subjects.

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 control subjects 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 10% or were significantly associated with disease status in our population: skin color, family history of melanoma and/or NMSC, first exposure of the season to 1 hour of summer sun, prolonged exposure to the sun, and *MC1R* nonsynonymous 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 or larger on back, freckles on face, body mass index, 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 because of the skewed nature of the exposures (eg, tanning sessions, tanning hours), the ordinal scores appeared more appropriate and are presented here. This was supported by a goodness-of-fit test ( $\chi^2$  distribution with  $k-2$  degrees of freedom) taking the difference between the  $\chi^2$  statistic from the model with  $k-1$  variables for each exposure (where  $k$  = number of exposure categories) and the  $\chi^2$  statistic for a model with the: (1) ordinal categorical variable; and (2) median scored variable.<sup>30</sup>

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 patients exposed ( $E$  = exposure,  $D$  = disease) and  $RR$  = relative risk approximated by the OR based on the rare disease assumption.<sup>30</sup> All descriptive and multivariate analyses were conducted using software (SAS, Version 9.2, SAS Institute Inc, 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. Patients with BCC 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 control subjects (Table I). Patients were also more likely to have never smoked, have normal body mass indices and have attained higher education levels compared with control subjects.

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 control subjects with the 3 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 3 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 ( $\leq 16$  years OR 1.83, 95% CI 1.12-2.97) as compared with 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 < .001) and number of burns specifically to the biopsy site ( $P$  trend < .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 = .003), with those who tanned indoors for 6 or more years greater than 2-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 = .030) and high-pressure ( $P$  trend = .004) tanning beds/booths were also positively linearly associated with BCC (data not shown).

Female participants who tanned indoors were approximately two times more likely to have a BCC compared with female never indoor tanners (OR 2.14, 95% CI 1.31-3.47), whereas among males 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 2-fold and 4-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 ( $P_{\text{interaction}}$  = .012; OR 2.81, 95% CI 1.57-5.02). We observed stronger associations for ever indoor tanning among females by body site; nonsignificant 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 nonsynonymous *MC1R* variants (OR 1.99, 95% CI 1.28-3.09), although the gene-environment interaction was not significant ( $P_{\text{interaction}}$  = .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 with fair or olive skin (OR 1.56, 95% CI 0.99-2.46), but this interaction was also

**Table 1.** Selected characteristics among non-Hispanic white patients with basal cell carcinoma and control subjects in Yale Study of Skin Health in Young People (N = 766)

Characteristic	Cases, N = 376 N*	Controls, N = 390 N*	P value†
Age (y), median (IQR)	36.3 (33.2-38.5)	36.8 (32.8-38.5)	.923
Female	256 (68.1%)	274 (70.3%)	.515
Body site of skin biopsy			<.001
Head	204 (54.3%)	164 (42.1%)	
Extremity	72 (19.2%)	126 (32.3%)	
Trunk	100 (26.6%)	100 (25.6%)	
Education			.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			<.001
Brown	86 (22.9%)	154 (39.5%)	
Hazel	65 (17.3%)	72 (18.5%)	
Green	47 (12.5%)	38 (9.7%)	
Blue/gray	178 (47.3%)	126 (32.3%)	
Hair color			<.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)			<.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			<.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			<.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)	.004
Freckles on face			<.001
None	78 (20.7%)	139 (35.6%)	
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 nonsynonymous variants			<.001
0	65 (17.3%)	131 (34.2%)	
1	173 (46.1%)	175 (45.7%)	
≥ 2	137 (36.5%)	77 (20.1%)	
Family history of skin cancer	246 (65.4%)	153 (29.2%)	<.001
Body mass index, kg/m <sup>2</sup>			<.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%)	<.001
Ever drank alcohol ≥ once/wk for ≥ 6 mo	282 (76.2%)	277 (71.9%)	.181

Continued



**Table I.** Cont'd

Characteristic	Cases, N = 376 N <sup>a</sup>	Controls, N = 390 N <sup>a</sup>	P value <sup>†</sup>
Smoking status			<.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	.010 <sup>‡</sup>
Outdoor activities (h), median (IQR)	6825 (3286-11,397)	6260 (3204-11,475)	.431
Sunburns (n), median (IQR)	6 (1-16)	3 (1-9)	<.001
Sunbathing sessions (n), median (IQR)	315 (58-713)	279 (84-689)	.622
Employed in outdoor job (mo), median (IQR)	0 (0-12)	0 (0-10)	.265

IQR, Interquartile range; MC1R, melanocortin 1 receptor gene.

<sup>a</sup>May not sum to total because of missing values.

<sup>†</sup> $\chi^2$  For categorical variables, Wilcoxon rank sum for continuous variables.

<sup>‡</sup>t Test.

not significant ( $P_{\text{interaction}} = .730$ ). 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 BCCs could be prevented if individuals never tanned indoors. Among females younger than 40 years, the proportion of preventable cases was even higher, with 43% of BCCs avoided if female participants 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 patients with multiple BCCs and more pronounced for females, as female indoor tanners were two times more likely to have BCC than females 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 with lesions on the head/neck, which receive considerable incidental UV exposure.

Before this investigation, research on indoor tanning and BCC (summarized in Table IV) had largely been in older populations,<sup>20-25</sup> with only two small studies of early-onset BCC.<sup>26,27</sup> The prevalence of indoor tanning in studies of patients with BCC 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% nonsignificant increased risk for skin malignancies on the head/neck<sup>31</sup> and null results for NMSC in two hospital case-control studies.<sup>32,33</sup>

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).<sup>17</sup> However, much of the melanoma literature and many studies of indoor tanning and NMSC 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, and dose-response relationships.<sup>34,35</sup> 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,<sup>34,35</sup> 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<sup>17</sup> and early-onset melanoma,<sup>35</sup> with a suggestive trend for BCC.<sup>20</sup> However, other evidence suggests a similar melanoma risk regardless of the age at initiation.<sup>34</sup> 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 younger and half reported their first use at age 17 or younger.

In our sample, indoor tanning was much more common and frequent among females, and our

**Table II.** Odds ratios and 95% confidence intervals for association between indoor tanning and early-onset basal cell carcinoma in Yale Study of Skin Health

Characteristic	Cases/controls	Minimally adjusted OR* (95% CI)	Cases/controls	Multivariate OR† (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‡		.388		.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‡		.292		.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‡		<.001		<.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‡		<.001		<.001
Ever used tanning bed/booth				
Regular	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)
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‡		.057		.003

For all variables, referent group is never indoor tanning.

CI, Confidence interval; OR, odds ratio.

\*Adjusted for frequency matching study variables: age at diagnosis, body site, and gender.

†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 nonmelanoma skin cancer (yes, no), first exposure of season to 1 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 sun (very brown and deeply tanned, moderately tanned, only mildly tanned because of tendency to peel, only freckled or no suntan at all), and melanocortin 1 receptor gene nonsynonymous variants (0, 1, ≥ 2).

‡Based on ordinal categorical variables.

population being predominantly female limited our ability to examine the association in male participants. The stronger effect of indoor tanning in

females is likely caused by a number of factors, including earlier age at initiation, greater number of tanning sessions (more individuals with greater

**Table III.** Odds ratios and 95% confidence intervals for association between indoor tanning and basal cell carcinoma in Yale Study of Skin Health stratified by selected characteristics

Characteristic	Indoor tanning	Cases/controls	Multivariate OR* (95% CI)	P for interaction <sup>†</sup>
Gender				.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				.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 nonsynonymous variants				.194
0	Never	25/45	1.00	
	Ever	40/85	1.09 (0.50-2.38)	
≥ 1	Never	104/92	1.00	
	Ever	206/160	1.99 (1.28-3.09)	
Skin color				.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)	

CI, Confidence interval; MC1R, melanocortin 1 receptor gene; OR, odds ratio.

\*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 nonmelanoma skin cancer (yes, no), first exposure of season to 1 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 sun (very brown and deeply tanned, moderately tanned, only mildly tanned because of tendency to peel, only freckled or no suntan at all), and MC1R nonsynonymous variants (0, 1, ≥ 2).

<sup>†</sup>Based on inclusion of cross-product term in multivariate model.

exposure), and a larger proportion of females with tumors located on the trunk and extremities, which were more strongly related to indoor tanning in our data. Although exposure differences are the most likely explanation for the gender difference, some of the observed effects could be caused by other unidentified factors and should be investigated in future larger or pooled studies. Of note, among males we saw the same pattern by body site, with elevated, although nonsignificant, 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 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 nonsynonymous 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 patients with BCC possibly underreporting overall indoor tanning. Although the impact of these potential biases on our results are unknown, the percentage of patients and control subjects (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.<sup>36-38</sup>

Our study had several important strengths including adequate power, particularly among females, to examine the relationship between BCC and indoor tanning in an extremely relevant population, and 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



**Table IV.** Summary of research on indoor tanning and/or sunlamps and risk of basal cell carcinoma

Reference	Country	Population	Cases/ controls	Prevalence or measure of indoor tanning in cases	OR* (95% CI)
Early-onset BCC					
Bakos et al <sup>26</sup>	Germany	Men and women, age 19-40 y, hospital-based sample	25/25	Regular use of tanning beds = 68%	25.0 (2.26-277.36)
Boyd et al <sup>27</sup>	US	Women age 20-40 y, 1 university dermatopathology division	30/30	Average No. of indoor tanning sessions = 152.2	OR not reported, <i>P</i> = .35 for difference in mean No. of sessions
Current article	US	Men and women, age <40 y, university dermatopathology facility serving dermatologists in Connecticut	375/382	Ever indoor tanning = 66%	1.69 (1.15-2.48)
Patients not selected for age at onset					
Bajdik et al <sup>22</sup>	Canada	Men age 25-79 y, population-based sample from Alberta	226/404	Ever use of sunlamps = 10%	1.2 (0.7-2.2)
Corona et al <sup>23</sup>	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 <sup>24</sup>	US	Women, age 43-68 y 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 <sup>20</sup>	US	Men and women, age 25-74 y, population-based sample	601/539	Ever indoor tanning = 21%	1.5 (1.1-2.1)
Rosso et al <sup>25</sup>	Switzerland	Men and women, age 20-75 y, population-based sample from Sion	120/144	Ever use of sunlamps = 8.3%	1.24 (0.53-2.88)
Walther et al <sup>21</sup>	Germany	Men and women, case median age 69 y, hospital-based sample	213/411	Use of artificial UV radiation or UV beds >5 times/y = 4%	0.7 (0.3-1.5) Unadjusted for >5 vs ≤5 times/y

BCC, Basal cell carcinoma; CI, confidence interval; OR, odds ratio; US, United States; UV, ultraviolet.

\*Multivariate, unless noted otherwise.

design limited the potential for interviewer bias, and because control subjects had also undergone skin biopsy, the potential for differential recall of behaviors by case status may have been minimized. In addition, by identifying patients and control subjects from a centralized dermatopathology facility serving many dermatologists in Connecticut, our control subjects represent the source population of our patients, that is, young people who see a dermatologist for a skin condition. Because study participants were all younger than 40 years 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 caused, in part, by other unmeasured factors or residual confounding. Arguing against this, we considered known correlates of indoor tanning<sup>18</sup> 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 younger than 40 years 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 younger than 40 years. Our control subjects 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 use indoor tanning to a greater extent. Although population-based control subjects are often sought in case-control studies, because our patients either sought out or were referred for dermatologic evaluation for a lesion when they were younger than 40 years, which could track with factors such as socioeconomic status or insurance status that may also be correlated with tanning, population-based control subjects could also have introduced bias.

Indoor tanning was a strong risk factor for BCC in a population of individuals younger than 40 years. We observed stronger associations in females 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.<sup>39</sup> Although 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 specifically 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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