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Original Contribution

Indoor Tanning and Melanoma Risk: Long-Term Evidence From a Prospective Population-Based Cohort Study

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Indoor tanning is associated with increased risk of melanoma, but most evidence comes from case-control studies. Using data from the Norwegian Women and Cancer Study, a large prospective cohort study, we investigated the associations of age at initiation of indoor tanning, duration of tanning-device use, and dose response with melanoma risk and examined the role of indoor tanning in age at melanoma diagnosis. We used Poisson regression to estimate relative risks and 95% confidence intervals for the relationship of indoor tanning to melanoma risk and linear regression to examine age of indoor tanning initiation in relation to age at diagnosis. During follow-up of 141,045 women (1991–2012; mean duration follow-up = 13.7 years), 861 women were diagnosed with melanoma. Melanoma risk increased with increasing cumulative number of tanning sessions (for highest tertile of use vs. never use, adjusted relative risk = 1.32, 95% confidence interval (CI): 1.08, 1.63); *P*-trend = 0.006. Age at initiation <30 years was associated with a higher risk in comparison with never use (adjusted relative risk = 1.31, 95% CI: 1.07, 1.59). Moreover, women who started indoor tanning prior to 30 years of age were 2.2 years (95% CI: 0.9, 3.4) younger at diagnosis, on average, than never users. This cohort study provides strong evidence of a dose-response association between indoor tanning and risk of melanoma and supports the hypothesis that vulnerability to the harmful effects of indoor tanning is greater at a younger age.

cohort studies; indoor tanning; melanoma; Norway; prospective studies; tanning beds; ultraviolet radiation

Abbreviations: CI, confidence interval; IARC, International Agency for Research on Cancer; NOWAC, Norwegian Women and Cancer; RR, relative risk; UV, ultraviolet; UVA, ultraviolet A; UVB, ultraviolet B.

Editor's note: *An invited commentary on this article appears on page 157, and the authors' response appears on page 160.*

The incidence of cutaneous melanoma (hereafter termed melanoma) has increased dramatically during the past few decades among fair-skinned populations worldwide; there were an estimated 230,000 new cases and 55,000 deaths in 2012 (1). In Norway, melanoma has gone from being uncommon in the 1950s to being the fourth most common incident cancer among both men and women in the last decade; as of 2014, the incidence rate was 42 cases per 100,000 population per year in men and 37 cases per 100,000 population per year in women (2).

The relationship between indoor tanning and melanoma has been investigated in several case-control studies and a few cohort studies, and the most recent meta-analyses found that ever users of indoor tanning devices had a 16%–20% higher risk of melanoma than nonusers (3, 4). However, these summary estimates were mainly based on case-control studies, and high-quality evidence remains scarce (4, 5).

In 2009, the International Agency for Research on Cancer (IARC) classified ultraviolet (UV) radiation from indoor tanning devices as carcinogenic to humans (6, 7). Despite this, indoor tanning has remained popular in many Western

countries, especially among young people (8). In a meta-analysis of the most recent international data (2007–2012), past-year prevalence of indoor tanning was 18% among adults and 45% among university students (8). In a Norwegian survey from 2014, past-year prevalence of indoor tanning was 16% in adults (9).

The Norwegian Women and Cancer (NOWAC) Study, a large, well-characterized, population-based cohort study with exposure information updated during follow-up, provides a unique opportunity to prospectively examine the long-term risk of melanoma in relation to indoor tanning. We studied the associations of current use, age at indoor tanning initiation, duration of use, and dose response with melanoma risk. In addition, we examined the role of indoor tanning in age at melanoma diagnosis.

METHODS

The NOWAC study sample

The NOWAC cohort includes women born in 1927–1965. Enrollment started in 1991. Details on the study population and the NOWAC study design have been published previously (10). Briefly, nationwide random samples of more than 300,000 women aged 30–75 years were drawn from the Norwegian National Population Register. All women received an invitation letter between 1991 and 2007, and 171,725 answered the questionnaire and gave written informed consent to participate (response rate = 54%).

Answers to detailed questions about host characteristics and UV exposure were collected for 162,834 women (born in 1927–1957) at baseline (Figure 1). The participants received follow-up questionnaires every 4–6 years. The first 57,000 women included in NOWAC in 1991/1992 were part of a separate study, the Norwegian-Swedish Women's Lifestyle and Health Cohort Study. That study formed the basis for previous analyses of melanoma risk factors (11, 12) but included only data from baseline questionnaires. In the current study, we evaluated melanoma risk in the entire NOWAC cohort and included exposure information obtained from the follow-up questionnaires.

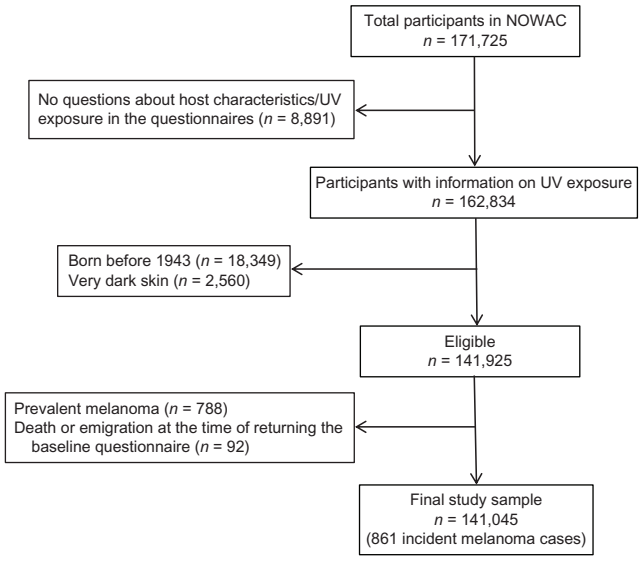

Figure 1. Selection of participants from the Norwegian Women and Cancer (NOWAC) Study cohort for an analysis of indoor tanning and melanoma risk, 1991–2012.

We excluded participants with very dark skin ($n = 2,560$), as well as 18,349 women born in 1927–1942 who had spent most of their lives prior to the availability of any indoor tanning devices (the first whole-body sunbed was introduced to the market in 1972 in Norway) (13). We further excluded participants with prevalent melanoma ($n = 788$) and persons who died or emigrated before the date of questionnaire return ($n = 92$). Thus, the final study sample comprised 141,045 women born in 1943–1957 (Figure 1).

Follow-up and endpoints

The unique 11-digit identity number assigned to Norwegian citizens was used to link individuals from NOWAC to the population register at Statistics Norway for information on postal address and to the Cancer Registry of Norway for follow-up of cancer incidence and vital status (alive, emigrated, or deceased) through December 31, 2012. Melanoma cases are registered according to the *International Classification of Diseases, Seventh Revision* (codes 190.0–190.9), and 99.9% of melanomas in the registry are morphologically verified (2). The Norwegian Data Inspectorate and the Regional Committee for Medical Research Ethics in North Norway approved the study.

Indoor tanning exposure

History of using an indoor tanning device was recorded for childhood (ages ≤9 years), adolescence (ages 10–19 years), and various age periods in adulthood, which varied between questionnaires (e.g., 20–29, 30–39, and 40–49 years in some questionnaires and 20–44 and ≥45 years in others). Participants were asked to report the average frequency of use of an indoor tanning device for the respective age periods as never, rarely, 1, 2, or 3–4 times per month, or >1 time per week. We created 5 variables to describe exposure to indoor tanning: cumulative number of indoor tanning sessions, ever/never use of tanning devices, duration of use (never, <10 years, or ≥10 years), current use (yes or no in the most recent age period), and age at indoor tanning initiation (never, <30 years, or ≥30 years, excluding a subsample of women who were asked about indoor tanning at ages 20–44 years ($n = 12,358$)).

To calculate the cumulative number of indoor tanning sessions, we converted the observed frequencies for all age periods starting from age 10 years to a yearly amount (never = 0 sessions/year; rarely = 1 session/year; 1 time/month = 12 sessions/year; 2 times/month = 24 sessions/year; 3–4 times/month = 42 sessions/year; and >1 time/week = 60 sessions/year) and multiplied this by the number of years for the given period; results were summed and categorized as never, lowest tertile (≤14 sessions), medium tertile (15–30 sessions), or highest tertile (≥31 sessions). Since very few participants

reported indoor tanning before age 10 years (<1%) and many did not answer the question on indoor tanning before age 10 years, we did not include this period in the calculation. Women with missing information for 1 or more age periods were considered to have missing data, and multiple imputations were used to impute missing values.

Covariates

We categorized region of residence (latitudes 70°N–58°N) according to average number of hours of ambient UV radiation (14) as low (northern Norway), medium-low (central Norway), medium (southwestern Norway), or high (southeastern Norway). We categorized number of years of education as ≤10, 11–13, or ≥14. Host factors included untanned skin color, hair color (black/dark brown, brown, blond/yellow, or red), freckling when sunbathing (yes, no), and number of asymmetrical nevi greater than 5 mm in diameter on the legs (0, 1, 2–3, 4–6, 7–12, 13–24, or ≥25; categorized as 0, 1, or ≥2). Untanned skin color was self-reported by participants using a 1- × 9-cm color scale graded from 1 (very fair) to 10 (very dark brown; very dark grades (grades 8–10) were excluded from the study) and was categorized as dark (grades 6 and 7), medium (grades 4 and 5), or light (grades 1–3). Annual number of severe sunburns that resulted in pain or blisters and subsequent peeling (never, 1, 2–3, 4–5, or ≥6) and average number of weeks per year spent on sunbathing vacations (never, 1 week/year, 2–3 weeks/year, 4–6 weeks/year, or ≥7 weeks/year) at low latitudes (typically Southern European countries with latitudes below 45°N, such as Spain or Greece) or within Norway or other northern countries were reported for the same age periods as for indoor tanning.

Cumulative number of sunburns was calculated in the same way as cumulative number of indoor tanning sessions but included the age period <10 years, and it was categorized as none, lowest tertile (≤30 sunburns), medium tertile (31–51 sunburns), or highest tertile (≥52 sunburns). Cumulative number of weeks spent on sunbathing vacations was calculated in the same way and was categorized as none, lowest tertile (≤46 weeks), medium tertile (47–87 weeks), or highest tertile (≥88 weeks). Finally, we calculated cumulative number of indoor and outdoor tanning sessions by summing tertiles of cumulative number of indoor tanning sessions and cumulative number of sunbathing vacations (score ranged from 0–6) and categorizing the variable into 4 groups (1 = lowest, 4 = highest).

Information on indoor tanning, sunburns, and sunbathing vacations was updated through the follow-up questionnaires. The reproducibility of most of the questions was assessed and shown to be good/acceptable; reproducibility was not affected by age, education, or skin color (15). The reliability coefficients for indoor tanning and sunbathing vacations at southern latitudes were 0.70 and 0.71, respectively.

Statistical analysis

Poisson regression analysis with age as the time scale was used to estimate relative risks and 95% confidence intervals for melanoma risk in relation to indoor tanning variables. Person-years were calculated from the date of return of the baseline questionnaire to the date of melanoma diagnosis, emigration, death, or the end of follow-up (December 31, 2012), whichever occurred first. Dynamic exposure variables (i.e., cumulative use, ever use, duration of use, and current use of indoor tanning), as well as cumulative numbers of sunburns and sunbathing vacations, were included as time-varying variables in all models. The association between indoor tanning and melanoma risk was examined by anatomical site (for the trunk and extremities but not the head/neck, because of few cases) and by histological subtype (for superficial spreading melanoma and nodular melanoma but not for other subtypes, because of few cases).

All analyses included adjustment for attained age (in 5-year intervals), birth cohort (1943–1957), and calendar year of study entry (1991, 1992, 1997, 1998, or 2004–2007), since calendar year of indoor tanning exposure may influence the level of UV irradiance (16). In the second model, we further adjusted for residential ambient UV exposure, hair color, and cumulative numbers of sunburns and sunbathing vacations. Additional adjustment for skin color, number of asymmetrical nevi, and freckling when sunbathing did not change the results.

In calculating the cumulative number of indoor tanning sessions, 15% (n = 21,037) of the observations had missing information for 1 or more age periods. In addition, in the multivariable analysis, approximately 15% of participants were missing information on 1 or more covariates. Thus, we used multiple imputation with chained equations (17), imputing 15 data sets to evaluate the influence of missing information on the estimates. The imputation models included all of the covariates included in the second model, and the results are presented as those of model 3. We tested the trend of association with a variable across categories by treating the variable as continuous in the model. Interaction effects between cumulative number of indoor tanning sessions and duration of use (<10 years, ≥10 years), age at initiation (<30 years, ≥30 years), cumulative number of sunburns (never, lowest tertile, or medium/highest tertiles), cumulative number of sunbathing vacations (never, lowest tertile, or medium/highest tertiles), birth cohort, freckling, hair color (dark, light), number of nevi (0, 1, or ≥2), and year of study entry were tested with a likelihood ratio test.

We studied the association between age at indoor tanning initiation and age at diagnosis using linear regression analysis. Results are presented as regression-coefficient estimates ($\hat{\beta}$) and 95% confidence intervals. The multivariable model included birth cohort, year of study entry, hair color, and cumulative numbers of sunburns and sunbathing vacations. We further conducted the same analysis with cases confined to early-onset melanomas (women diagnosed at age <50 years; n = 137). We used 2-sided statistical tests and a 5% significance level. Stata, version 14 (StataCorp LP, College Station, Texas) was used in all analyses.

RESULTS

Study sample and indoor tanning

We included 141,045 women in the analysis, and 861 women were diagnosed with incident melanoma during

1,930,583 person-years of follow-up (mean duration of follow-up = 13.7 years). Mean age at study entry was 48 years (range, 34–64), and mean age at diagnosis was 56 years (range, 34–69). The lower limb was the most common site of melanoma (n = 343), followed by the trunk (n = 303), upper limb (n = 116), head/neck (n = 52), and multiple sites/unspecified (n = 47). The majority of cases were superficial spreading melanoma (61%) and nodular melanoma (14%).

Ever use of indoor tanning devices was reported by 70% of the participants (Table 1). Indoor tanning was more common among women in the younger birth cohorts, women living in southeastern Norway (which had the highest level of residential ambient UV exposure), women with fewer years of education, women with a light skin color, and women who reported a higher cumulative number of sunbathing vacations (Table 1). In general, very few women reported indoor tanning when aged 10–19 years, and frequent use of tanning devices at this age was not common even among women in the highest tertile of cumulative number of indoor tanning sessions (Figure 2). There was a tendency toward a higher proportion of women reporting indoor tanning initiation before age 30 in the younger birth cohorts (Figure 3).

Indoor tanning and melanoma risk

Results from complete-case and multiple-imputation analyses were similar. Estimates from the multiple-imputation analysis are reported here, except P values for interaction.

Ever users of indoor tanning devices had a significantly higher risk of melanoma than never users (adjusted relative risk (RR) = 1.24, 95% confidence interval (CI): 1.05, 1.46; Table 2). Compared with women who reported no current use of indoor tanning devices, current users were at a significantly higher risk of melanoma (adjusted RR = 1.27, 95% CI: 1.10, 1.47).

We found increased risks of melanoma for both women who initiated indoor tanning prior to age 30 years (adjusted RR = 1.34, 95% CI: 1.05, 1.66) and women who initiated indoor tanning at ages ≥30 years (adjusted RR = 1.15, 95% CI: 0.96, 1.35) in comparison with never users. Melanoma risk increased with increasing duration of use (P-trend = 0.009) (Table 2). Melanoma risk increased significantly with cumulative number of indoor tanning sessions (for the highest tertile of use compared with never use, adjusted RR = 1.32, 95% CI: 1.08, 1.63; P-trend = 0.006). The relative risk was even higher for a very high cumulative number of tanning sessions—for example, the relative risk was 1.53 (95% CI: 1.12, 2.09) among women with ≥480 sessions (e.g., 1 session per week on average for 10 years) compared with never users (results not shown). Testing for interaction between cumulative number of sessions and age at initiation showed a significantly higher melanoma risk among those with age at initiation <30 years (P-interaction = 0.02; Table 2). When we stratified the cumulative number of sessions by duration of use, the association between cumulative sessions and melanoma risk did not change (P-interaction = 0.71; results not shown). None of the associations between melanoma risk and cumulative tanning or ever indoor tanning varied by number of sunburns, sunbathing, birth cohort, freckling, number of nevi, hair color, or year of study entry ($0.09 < P$-interaction < 0.83). A highly significant trend in melanoma risk with increasing cumulative number of indoor and outdoor tanning sessions was observed (P-trend < 0.001).

Ever use, current use, duration of use, and cumulative number of sessions were associated with significantly increased risk of superficial spreading melanoma but not nodular melanoma, although confidence intervals around the relative risk for nodular melanoma were wide because of the limited number of cases (see Web Table 1, available at http://aje.oxfordjournals.org/). Site-specific analyses gave similar results for the trunk and extremities (Web Table 2).

Age at initiation and age at diagnosis

Mean age at diagnosis was significantly lower for both women who initiated tanning at age <30 years and women who initiated tanning at age ≥30 years than for never users (Table 3). In the adjusted analysis, compared with never users, mean age at diagnosis was 2.2 years (95% CI: 0.9, 3.4) lower among women who started indoor tanning at age <30 years and 1.2 years (95% CI: 0.2, 2.1) lower among women who started indoor tanning at age ≥30 years (Table 3). The analysis confined to early-onset melanomas (age <50 years) provided similar results, with wider confidence intervals due to few cases (results not shown).

DISCUSSION

In this large prospective cohort study of indoor tanning and melanoma risk, we found a significant dose-response association with cumulative number of indoor tanning sessions. Moreover, current use, younger age at initiation of indoor tanning, and longer duration of use were significantly associated with a higher risk of melanoma. Importantly, indoor tanning was associated with younger age at melanoma diagnosis. These associations remained significant after controlling for potential confounders, including age, birth cohort, residential ambient UV exposure, hair color, skin color, and cumulative numbers of sunburns and sunbathing vacations. We found a significantly higher risk of superficial spreading melanoma, the most commonly occurring histological subtype of melanoma in relation to indoor tanning use, but not a higher risk of nodular melanoma; this may have reflected the reduced statistical power to detect an association with the smaller number of cases of nodular melanoma.

We found a 32% increased risk of melanoma for women with cumulative totals of >30 tanning sessions (highest tertile), and risk was 53% higher for those with ≥480 sessions (e.g., once a week or more for 10 years, on average) compared with never use. Our findings support the evidence from 2 recent meta-analyses (3, 4). Two cohort studies found a nonsignificant or borderline-significant increased risk of melanoma among indoor tanners; however, those investigators did not have detailed information on indoor tanning, and the sample sizes were quite small (18, 19). To

Table 1. Characteristics of Participants in an Analysis of Indoor Tanning and Melanoma Risk, According to Cumulative Number of Indoor Tanning Sessions (n = 120,008), Norwegian Women and Cancer Study, 1991–2012

	Cumulative No. of Indoor Tanning Sessions							
	Never Use		Lowest Tertile (≤14 Sessions)		Medium Tertile (15–30 Sessions)		Highest Tertile (≥31 Sessions)	
	No.	%	No.	%	No.	%	No.	%
No. and % of participants[a]	35,405	29.5	20,891	17.4	30,864	25.7	32,848	27.4
Total person-years of follow-up	466,909		310,938		373,757		455,846	
Mean person-years of follow-up	13.2		14.8		12.1		13.8	
Incident melanoma cases[a]	199	26.2	151	19.9	184	24.2	225	29.6
Birth cohort								
1943–1947	13,182	37.2	5,733	27.4	8,792	28.5	10,629	32.4
1948–1952	11,322	32.0	6,223	29.8	10,017	32.5	11,190	34.1
1953–1957	10,901	30.8	8,935	42.8	12,055	39.0	11,029	33.6
Residential ambient UV exposure								
Low (northern Norway)	19,073	53.9	10,809	51.7	14,623	47.4	16,044	48.8
Medium-low (central Norway)	8,281	23.4	4,376	20.9	5,879	19.0	4,870	14.8
Medium (southwestern Norway)	3,254	9.2	2,395	11.6	3,866	12.5	3,868	11.8
High (southeastern Norway)	4,797	13.5	3,311	15.8	6,496	21.1	8,066	24.6
Education, years								
≤10	10,458	29.5	5,636	27.0	8,202	26.6	10,451	31.8
11–13	9,045	25.5	6,169	29.5	9,601	31.1	10,534	32.1
≥14	14,410	40.7	8,412	40.3	11,819	38.3	10,402	31.7
Missing data	1,492	4.3	674	3.2	1,242	4.0	1,461	4.4
Skin color								
Dark	13,145	37.1	6,851	32.8	11,359	36.8	11,559	35.2
Medium	11,086	31.3	6,739	32.2	11,117	36.0	11,762	35.8
Light	5,694	16.1	3,774	18.1	5,836	18.9	6,445	19.6
Missing data[b]	5,480	15.5	3,527	16.9	2,552	8.3	3,082	9.4
Hair color								
Black/dark brown	6,659	18.8	3,464	16.6	4,898	15.9	4,786	14.6
Brown	13,918	39.3	8,501	40.7	12,798	41.5	13,587	41.4
Blond/yellow	13,331	37.7	8,123	38.9	12,082	39.1	13,300	40.5
Red	1,249	3.5	714	3.4	964	3.1	983	3.0
Missing data	248	0.7	89	0.4	122	0.4	192	0.5
Freckling when sunbathing								
No	20,321	57.4	11,188	53.6	18,404	59.6	19,061	58.0
Yes	10,382	29.3	6,650	31.8	10,454	33.9	11,322	34.5
Missing data[b]	4,702	13.3	3,053	14.6	2,006	6.5	2,465	7.5
Total no. of asymmetrical nevi with diameter >5 mm on legs								
0	28,899	81.6	17,537	83.9	25,567	82.8	26,590	80.9
1	2,113	6.0	1,344	6.5	1,925	6.2	2,224	6.8
≥2	1,550	4.4	944	4.5	1,412	4.6	1,802	5.5
Missing data	2,843	8.0	1,066	5.1	1,960	6.4	2,232	6.8
Tertile of cumulative no. of sunburns								
None	3,933	11.1	1,682	8.1	2,682	8.7	2,718	8.3
Lowest tertile (≤30 sunburns)	9,089	25.7	5,985	28.6	8,820	28.6	8,882	27.0
Middle tertile (31–51 sunburns)	8,007	22.6	5,432	26.0	7,268	23.5	7,871	24.0
Highest tertile (≥52 sunburns)	8,960	25.3	5,093	24.4	8,159	26.5	9,020	27.5
Missing data	5,416	15.3	2,699	12.9	3,935	12.7	4,357	13.2

Table continues

Table 1. Continued

	Cumulative No. of Indoor Tanning Sessions							
	Never Use		Lowest Tertile (≤14 Sessions)		Medium Tertile (15–30 Sessions)		Highest Tertile (≥31 Sessions)	
	No.	%	No.	%	No.	%	No.	%
Tertile of cumulative no. of sunbathing vacations								
None	3,872	10.9	861	4.1	620	2.0	509	1.5
Lowest tertile (≤46 weeks)	11,908	33.6	7,775	37.2	8,733	28.3	8,765	26.7
Middle tertile (47–87 weeks)	8,275	23.4	5,593	26.8	10,273	33.3	10,162	30.9
Highest tertile (≥88 weeks)	8,710	24.6	5,452	26.1	9,854	31.9	11,522	35.1
Missing data	2,640	7.5	1,210	5.8	1,384	4.5	1,890	5.8

Abbreviation: UV, ultraviolet.
[a] Percentages are row percentages.
[b] The relatively higher amount of missing data was due to the fact that the question was not included in all baseline questionnaires.

our knowledge, this study is the first prospective cohort study to have investigated cumulative number of indoor tanning sessions over several decades of life, as well as the relationship of current use and age at initiation to melanoma risk and average age at melanoma diagnosis.

Any indoor tanning was significantly associated with younger age at diagnosis, with a 2-year decrease in mean age at diagnosis among patients who started indoor tanning prior to 30 years of age. While this is the first study to have examined the association between indoor tanning and mean age at melanoma diagnosis, 2 case-control studies found a significant association between indoor tanning and early-onset melanoma. Those authors reported that participants with more than 10 indoor tanning sessions over the course of a lifetime

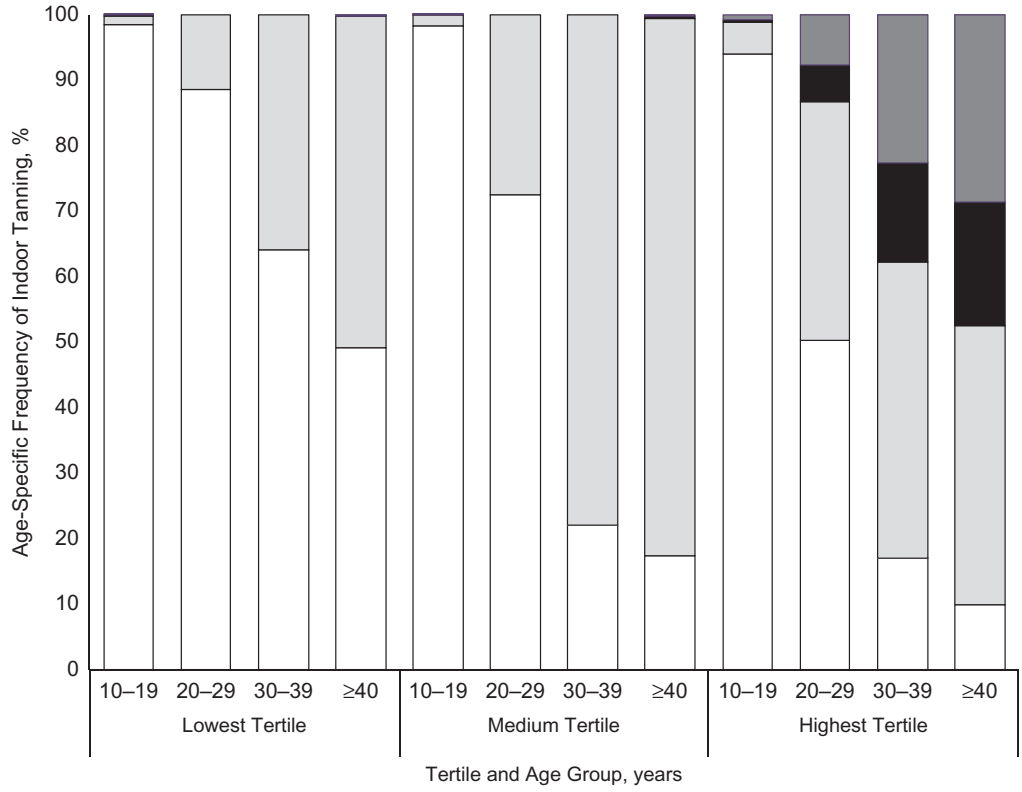

Figure 2. Reported frequency of indoor tanning by age of exposure and tertile of cumulative number of tanning sessions among participants in the Norwegian Women and Cancer Study (n = 120,008), 1991–2012. Women with missing data for 1 or more age periods were excluded (n = 21,037). White portions of the columns represent never use of tanning devices, light gray portions represent "rare" use (per the questionnaire), black portions represent use once per month, and dark gray portions represent use ≥2 times per month.

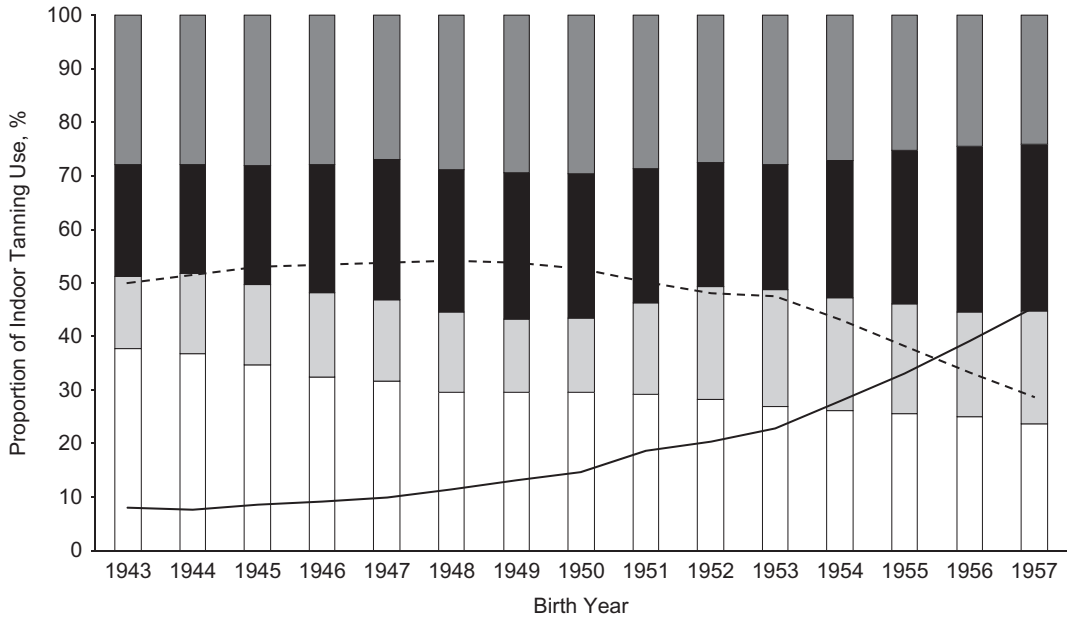

Figure 3. Cumulative number of indoor tanning sessions (never, lowest tertile, or medium/highest tertiles) and age at initiation of indoor tanning (<30 years, ≥30 years), by year of birth, among participants in the Norwegian Women and Cancer Study (n = 104,617), 1991–2012. The stacked columns represent tertile of cumulative number of indoor tanning sessions (white, never use of tanning devices; light gray, lowest tertile of use; black, medium tertile of use; dark gray, highest tertile of use). The dashed line represents the proportion of women who initiated indoor tanning at age ≥30 years; the solid line represents the proportion who initiated indoor tanning at age <30 years.

were at significantly higher risk of being diagnosed with melanoma before age 30 years (20, 21). The minimum age at inclusion in our study was 34 years, and we excluded melanomas diagnosed before study entry; thus, the difference in average age at diagnosis for indoor tanners compared with never users is likely to be larger than our estimates suggest. Considering the currently high prevalence of indoor tanning among young people, this finding has important implications for public health. It shows that indoor tanning increases the burden of melanoma not only by increasing its incidence but also by decreasing age at onset. Globally, it is estimated that 1,169,000 years of life were lost due to melanoma in 2010 (22), and a person dying from melanoma loses an average of 20 years of potential life (23, 24).

In Norway, the first whole-body tanning device became available in 1972, and indoor tanning became popular during the 1980s (13). Thus, most of our study cohort (born in 1943–1957) did not have access to sunbeds during their adolescence. The prevalence of indoor tanning was high among these participants, with 70% reporting ever tanning indoors, but the cumulative number of sessions was quite low, and two-thirds of the indoor tanners reported ≤30 sessions. The proportion of indoor tanners with age at initiation <30 years was approximately 20% in our study, with an increasing trend in the younger cohorts. According to a recent Norwegian survey, 35% of respondents aged 18–24 years reported having engaged in indoor tanning during the past year (9), and in a recent meta-analysis, Wehner et al. (8) reported indoor tanning among 55% of university students, with 43% engaging in indoor tanning during the past year and a significant increasing trend over time. At the same time, in a recent systematic review, Nilsen et al. (25) found a trend toward a significantly higher level of UV radiation being measured in modern indoor tanning devices in recent years in Europe, and the level of this UV radiation is higher than that from natural sunlight. Therefore, younger generations are being exposed to a higher dose of artificial UV radiation than the women in our study cohort, and the negative impact of indoor tanning among them would be expected to be higher than that observed in our cohort.

In 1983, Norway implemented the first regulations on indoor tanning devices. At that time, tanning devices with lamps rich in ultraviolet B (UVB) radiation were replaced by devices with ultraviolet A (UVA)-rich fluorescent lamps (13). Thus, in our study, older birth cohorts were more exposed to UVB-rich tanning devices and younger birth cohorts were mainly exposed to newer, UVA-rich devices. However, we found no interaction in the association between indoor tanning and melanoma risk by birth cohort, which is in line with the evidence from other studies that newer tanning devices are as hazardous as the older ones (19, 26, 27).

In its 2006 meta-analysis, IARC found a higher melanoma risk associated with younger age at tanning initiation (≤35 years) and suggested that there may be greater susceptibility to harmful effects of indoor tanning during youth (28). However, the literature is not conclusive in this regard. In a recent report, Lazovich et al. (29) suggested that early age at initiation of indoor tanning is most likely a marker

Table 2. Relative Risk of Melanoma According to Exposure to Indoor Tanning Devices Among Participants in the Norwegian Women and Cancer Study, 1991–2012[a]

Indoor Tanning Variable	Complete-Case Analysis							Multiple-Imputation Analysis (Model 3[d])	
	No. of Participants	%	No. of Cases	Model 1[b]		Model 2[c]			
				RR	95% CI	RR	95% CI	RR	95% CI
Ever engaging in indoor tanning	116,975		746						
Never tanning	34,122	29.2	203	1.00	Referent	1.00	Referent	1.00	Referent
Ever tanning	82,853	70.8	543	1.21	1.02, 1.42	1.24	1.05, 1.46	1.24	1.04, 1.44
Current use of indoor tanning devices	122,590		759						
No	57,659	46.9	317	1.00	Referent	1.00	Referent	1.00	Referent
Yes	64 931	53.1	442	1.17	1.01, 1.35	1.21	1.05, 1.40	1.27	1.10, 1.47
Age of initiation of use of indoor tanning devices, years	104,617		672						
Never use	30,774	29.4	185	1.00	Referent	1.00	Referent	1.00	Referent
≥30	53,396	51.1	358	1.16	0.97, 1.38	1.15	0.96, 1.37	1.15	0.96, 1.35
<30	20,447	19.5	129	1.36	1.08, 1.79	1.36	1.07, 1.73	1.34	1.05, 1.66
Duration of use of indoor tanning devices, years	116,975		746						
Never use	34,122	29.2	203	1.00	Referent	1.00	Referent	1.00	Referent
<10	17,140	14.6	141	1.17	0.94, 1.45	1.17	0.94, 1.46	1.18	0.95, 1.46
≥10	65,713	56.2	402	1.23	1.03, 1.46	1.27	1.06, 1.52	1.29	1.09, 1.54
P-trend[e]					0.022		0.009		0.009
Tertile of cumulative no. of tanning sessions	116,975		746						
Never use	34,122	29.2	203	1.00	Referent	1.00	Referent	1.00	Referent
Lowest tertile	20,527	17.5	158	1.15	0.93, 1.42	1.16	0.94, 1.43	1.19	0.96, 1.47
Medium tertile	30,229	25.9	177	1.21	1.00, 1.50	1.26	1.04, 1.58	1.26	1.03, 1.54
Highest tertile	32,097	27.4	208	1.25	1.02, 1.51	1.30	1.06, 1.58	1.32	1.08, 1.63
P-trend[e]					0.024		0.006		0.006
Age of tanning initiation and tertile of cumulative no. of tanning sessions	104,617		672						
≥30 years									
Never use	30,774	29.4	185	1.00	Referent	1.00	Referent	1.00	Referent
Lowest tertile	16,473	15.7	123	1.06	0.84, 1.34	1.03	0.82, 1.29	1.07	0.83, 1.33
Medium or highest tertile	36,923	35.3	235	1.21	1.00, 1.47	1.22	1.01, 1.49	1.22	1.01, 1.50
<30 years									
Never use	30,774	29.4	185	1.00	Referent	1.00	Referent	1.00	Referent
Lowest tertile	2,589	2.5	24	1.78	1.15, 2.74	1.78	1.16, 2.75	1.73	1.15, 2.64
Medium or highest tertile	17,858	17.1	105	1.30	1.01, 1.66	1.32	1.03, 1.69	1.31	1.07, 1.59
P-interaction (age group × tertile)[f]					0.025		0.016		
Quartile of cumulative no. of indoor and outdoor tanning sessions	116,975		746						
1 (lowest)	17,644	15.1	103	1.00	Referent	1.00	Referent	1.00	Referent
2	17,602	15.0	115	1.21	0.92, 1.59	1.20	0.91, 1.57	1.19	0.91, 1.56
3	49,817	42.6	336	1.50	1.20, 1.88	1.49	1.19, 1.87	1.47	1.18, 1.84
4 (highest)	31,912	27.3	192	1.62	1.26, 2.07	1.59	1.24, 2.04	1.61	1.27, 2.05
P-trend[e]					0.001		0.001		0.001

Abbreviations: CI, confidence interval; RR, relative risk.

[a] Poisson regression.

[b] Complete-case analyses with adjustment for attained age, birth cohort, and year of study entry.

[c] Complete-case analyses with adjustment for attained age, birth cohort, year of study entry, residential ambient ultraviolet radiation exposure, hair color, and cumulative number of sunburns and sunbathing vacations (additional adjustment for skin color, number of nevi, and freckling when sunbathing did not change the results).

[d] Analysis with multiple imputation of missing covariate data conducted using chained equations and a total of 15 generated data sets (n = 141,045; 861 cases). Results were adjusted for all of the variables in model 2.

[e] Test for linear trend conducted by treating the variables as continuous in the model.

[f] Test of the hypothesis that RR[age of initiation (AOI) ≥30 years and lowest tertile of cumulative sessions (TCS)] + RR(AOI ≥30 years and medium/highest TCS) = RR(AOI <30 years and lowest TCS) + RR(AOI <30 years and medium/highest TCS).

Table 3. Mean Age Differences in the Association Between Age at Initiation of Indoor Tanning and Age at Melanoma Diagnosis in the Norwegian Women and Cancer Study, 1991–2012[a]

Age at Initiation of Tanning, years	Mean Difference in Age at Diagnosis, years							
	Complete-Case Analysis						Multiple-Imputation Analysis	
	No. of Cases (n = 672)	Mean Age at Diagnosis (SD)	Crude $\hat{\beta}$ for Age Difference	95% CI	Adjusted $\hat{\beta}$[b]	95% CI	Adjusted $\hat{\beta}$[c]	95% CI
Never use	185	56.4 (6.0)	0	Referent	0	Referent	0	Referent
≥30	358	55.9 (6.5)	−0.5	−1.7, 0.7	−1.1	−2.1, −0.2	−1.2	−2.1, −0.2
<30	129	51.6 (7.5)	−4.8	−6.4, −3.3	−2.1	−3.4, −0.8	−2.2	−3.4, −0.9

Abbreviations: CI, confidence interval; SD, standard deviation.

[a] Linear regression analysis.

[b] Complete-case analysis with adjustment for birth cohort, year of study entry, hair color, and cumulative numbers of sunburns and sunbathing vacations.

[c] Multiple-imputation analysis with adjustment for all variables in the complete-case analysis (n = 689 cases). Multiple imputation of missing covariate data was conducted using chained equations and a total of 15 generated data sets.

for cumulative exposure, not an indication of increased susceptibility for younger people. However, in the report by Cust et al. (20), cumulative exposure did not fully account for the association between earlier age at initiation and melanoma risk. The higher risk of melanoma for initiation at age <30 years compared with initiation at age ≥30 years observed in our study provides supporting evidence of greater susceptibility during youth and young adulthood.

Since it is not ethical to use randomized controlled trials for investigating the association between indoor tanning and melanoma risk, large prospective cohort studies provide the highest level of evidence. NOWAC is a large, well-characterized, population-based prospective cohort study. Possession of detailed exposure information across several decades of life that was updated during follow-up, complete follow-up through high-quality national registries, and the large number of cases, with 99.9% of melanomas being morphologically verified (2), were some of the strengths of our study. However, a limitation is that the information on exposure at young ages was collected retrospectively. Thus, some misclassification of exposure is likely to have occurred, but it was most probably nondifferential, since all of the information was collected before melanoma diagnosis. We also did not collect information on the types of indoor tanning devices used and the duration of each tanning session; however, other studies found no difference in the risk by type of device (29–31). This study included only women aged ≥34 years. Although indoor tanning is more popular among women than among men (32, 33), another study found similar estimates for the association between indoor tanning and melanoma for men and women (29).

In summary, this large prospective cohort study provides strong supporting evidence on the strength, dose response, and temporality of the association between indoor tanning and melanoma risk. Moreover, our findings support the IARC's conclusion of a higher vulnerability to the harmful effects of indoor tanning before 35 years of age.

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