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Smoking behavior and association of melanoma and nonmelanoma skin cancer in the Women's Health Initiative

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To the Editor

Whereas smoking is associated with increased risk of most cancers, observational studies have suggested a lower risk with malignant melanoma (MM) and are inconsistent for non-melanoma skin cancer (NMSC).^{1–4} Using a large, prospective cohort of the Women's Health Initiative observational study, we evaluated the relationships of smoking to MM and NMSC. Incidence of MM and NMSC in current smokers was compared with incidence in never smokers and past smokers.

A total of 514 MM cases and 9046 NMSC cases were identified during a mean follow-up period of 11 years (Table I; available at <http://www.jaad.org>). Approximately 51% of women were never smokers, 43.5% reported being past smokers, and 5.6% were current smokers. Compared with never smokers, current smokers had lower odds of developing MM (hazard ratio 0.55, 95% confidence interval [CI] 0.32–0.94, $P_{\text{global}} = .053$) and NMSC (odds ratio 0.86, 95% CI 0.77–0.96, $P_{\text{global}} = .033$) in fully adjusted models; past smokers, however, did not differ with respect to MM (hazard ratio 1.06, 95% CI 0.88–1.27) or NMSC (odds ratio 0.99, 95% CI 0.95–1.04) risk (Table II).

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Conflicts of interest: None declared.

When stratified by duration and quantity of smoking, according to pack years for current and past smokers ($N = 27,597$), there was no significant trend overall between increasing pack years and risk of incident NMSC or MM. However, each 10-year increase in pack years smoked was associated with a small, but significant, 2% decrease in risk on NMSC ($P = .010$).

In this large cohort of older Caucasian women, we observed lower odds of both melanoma and NMSC among current smokers compared with lifelong nonsmokers. These results corroborate previous research suggesting an inverse relationship³ between cigarette smoking and melanoma while differing from null findings of past studies.⁴

An inverse relationship of smoking to skin cancer seems counterintuitive, given smoking's positive association with many other cancers⁵; however, this relationship persisted despite controlling for age, education, alcohol use, sun-exposure variables, and other potential confounders. One explanation for the lower odds of MM and NMSC in current smokers could be that "cancer-prone" individuals may succumb to other cancers at an earlier age than required for developing MM and NMSC and this fact may mask or skew the true rate of skin cancers in smokers (if all would have survived). We hypothesize that the observed lower skin cancer risk in smokers may be caused by detection bias related to lower screening for skin cancer in smokers. In fact, current smokers in the Women's Health Initiative are less likely to have medical insurance and are less likely to see physicians for cancer screening. Fewer current smokers ever had a mammogram (78% smokers vs 93% never smokers, respectively) or colonoscopy (46% of current smokers vs 56% of never smokers) (P value $< .0001$), similar to past studies on colorectal screening rates.⁵ Current smokers had lower rates of screening compared with never and past smokers despite having a current care provider and having insurance. In conclusion, smoking does not increase risk of skin cancer. Current smokers are associated with a lower risk of MM and NMSC possibly as a result of detection bias related to lower screening for skin cancer in smokers.

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Table 1

Baseline characteristics and outcomes by smoking status, no. (%)

Variable	Smoking status			Total	χ^2 P value
	Never	Past	Current		
Total	28,664 (51)	24,453 (43)	3144 (5.6)	56,261	
Age group					<.0001
<50–59 y	8763 (30)	7899 (32)	1290 (41)	17,952	
60–69 y	12,661 (44)	11,272 (46)	1384 (44)	25,317	
70– 79	7240 (25)	5282 (22)	470 (15)	12,992	
BMI category					<.0001
<25	12,666 (44.19)	10,383 (42.46)	1603 (50.99)	24,652	
25–<30	9585 (33.44)	8400 (34.35)	987 (31.39)	18,972	
30	6413 (22.37)	5670 (23.19)	554 (17.62)	12,637	
Ambient sun exposure, Langley					<.0001
300–325	9343 (32.59)	7991 (32.68)	930 (29.58)	18,264	
350	5989 (20.89)	5246 (21.45)	679 (21.60)	11,914	
375–380	3198 (11.16)	2501 (10.23)	343 (10.91)	6042	
400–430	4869 (16.99)	3740 (15.29)	466 (14.82)	9075	
475–500	5265 (18.37)	4975 (20.35)	726 (23.09)	10,966	
Skin reaction to the sun					<.0001
Does not burn	10,633 (37.10)	8053 (32.93)	1224 (38.93)	19,910	
Burns and tans	6718 (23.44)	6883 (28.15)	789 (25.10)	14,390	
Burns and tans minimally	7770 (27.11)	6864 (28.07)	789 (25.10)	15,423	
Burns and does not tan	3543 (12.36)	2653 (10.85)	342 (10.88)	6538	
Education					<.0001
High school	5846 (20.39)	4101 (16.77)	693 (22.04)	10,640	
Some college	9934 (34.66)	9095 (37.19)	1329 (42.27)	20,358	
College	12,884 (44.95)	11,257 (46.04)	1122 (35.69)	25,263	
History of NMSC					.49
No	25,939 (90.49)	22,100 (90.38)	2862 (91.03)	50,901	
Yes	2725 (9.51)	2353 (9.62)	282 (8.97)	5360	

Variable	Smoking status			Total	χ^2	P value
	Never	Past	Current			
History of melanoma						.61
No	28,248 (98.55)	24,114 (98.61)	3094 (98.41)	55,456		
Yes	416 (1.45)	339 (1.39)	50 (1.59)	805		
Childhood exposure to summer sun						<.0001
<30 min	706 (2.46)	480 (1.96)	60 (1.91)	1246		
30 min to 2 h	7734 (26.98)	6065 (24.80)	704 (22.39)	14,503		
>2 h	20,224 (70.56)	17,908 (73.23)	2380 (75.70)	40,512		
Current exposure to summer sun						<.0001
<30 min	8669 (30.24)	7541 (30.84)	1015 (32.28)	17,225		
30 min to 2 h	14,658 (51.14)	12,164 (49.74)	1433 (45.58)	28,255		
>2 h	5337 (18.62)	4748 (19.42)	696 (22.14)	10,781		
Usually use sunscreen outside						<.0001
No	13,599 (47.44)	10,641 (43.52)	1773 (56.39)	26,013		
Yes	15,065 (52.56)	13,812 (56.48)	1371 (43.61)	30,248		
Vitamin D from supplements, diet						<.0001
<400 IU	14,249 (49.71)	12,090 (49.44)	1852 (58.91)	28,191		
400 IU	14,415 (50.29)	12,363 (50.56)	1292 (41.09)	28,070		
Passive smoking exposure (any)						<.0001
None	2496 (8.71)	506 (2.07)	38 (1.21)	3040		
Exposure as child, adult at home, adult at work	26,168 (91.29)	23,947 (97.93)	3106 (98.79)	53,221		
Passive smoking exposure category						<.0001
None	2496 (8.71)	506 (2.07)	38 (1.21)	3040		
Child only	1754 (6.12)	403 (1.65)	37 (1.18)	2194		
Adult home only	1768 (6.17)	1227 (5.02)	87 (2.77)	3082		
Adult work only	3440 (12.00)	1228 (5.02)	108 (3.44)	4776		
>1	19,206 (67.00)	21,089 (86.24)	2874 (91.41)	43,169		
Pack years smoked						<.0001
20	28,664 (100.00)	15,371 (62.86)	1141 (36.29)	45,176		
>20	0 (0.00)	9082 (37.14)	2003 (63.71)	11,085		
Alcohol consumption						<.0001

Variable	Smoking status			χ^2	P value
	Never	Past	Current		
Nondrinker	4333 (15.12)	498 (2.04)	82 (2.61)	4913	
Past drinker	4527 (15.79)	4120 (16.85)	534 (16.98)	9181	
<1 drink/mo	3700 (12.91)	2323 (9.50)	434 (13.80)	6457	
<1 drink/wk	6283 (21.92)	4746 (19.41)	573 (18.23)	11,602	
1–<7 drinks/wk	7256 (25.31)	7968 (32.58)	809 (25.73)	16,033	
7 drinks/wk	2565 (8.95)	4798 (19.62)	712 (22.65)	8075	
Annual family income					<.0001
<\$20,000	3662 (12.78)	2723 (11.14)	589 (18.73)	6974	
\$20,000–\$35,000	6862 (23.94)	5315 (21.74)	804 (25.57)	12,981	
\$35,000–\$50,000	6004 (20.95)	5071 (20.74)	651 (20.71)	11,726	
\$50,000–\$75,000	5962 (20.80)	5402 (22.09)	606 (19.27)	11,970	
\$75,000	6174 (21.54)	5942 (24.30)	494 (15.71)	12,610	
Any insurance					<.0001
No	609 (2.12)	534 (2.18)	200 (6.36)	1343	
Yes	28,055 (97.88)	23,919 (97.82)	2944 (93.64)	54,918	
Last medical visit within 1 y					<.0001
No	4450 (15.52)	3617 (14.79)	664 (21.12)	8731	
Yes	24,214 (84.48)	20,836 (85.21)	2480 (78.88)	47,530	
Physical activity (metabolic equivalents min/wk)					<.0001
0–100	4969 (17.34)	3839 (15.70)	876 (27.86)	9684	
100–500	7595 (26.50)	5785 (23.66)	975 (31.01)	14,355	
500–1200	8922 (31.13)	7861 (32.15)	785 (24.97)	17,568	
1200	7178 (25.04)	6968 (28.50)	508 (16.16)	14,654	
Melanoma during follow-up					.002
No	28,417 (99.14)	24,200 (98.97)	3130 (99.55)	55,747	
Yes	247 (0.86)	253 (1.03)	14 (0.45)	514	
NMSC during follow-up					<.0001
No	24,085 (84.03)	20,405 (83.45)	2725 (86.67)	47,215	
Yes	4579 (15.97)	4048 (16.55)	419 (13.33)	9046	
Death during follow-up					<.0001

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Variable	Smoking status			Total	χ^2 P-value
	Never	Past	Current		
No	26,754 (93.34)	22,339 (91.35)	2686 (85.43)	51,779	
Yes	1910 (6.66)	2114 (8.65)	458 (14.57)	4482	

BMI, Body mass index; NMSC, nonmelanoma skin cancer.

Table II

Association of current smoking on melanoma or nonmelanoma skin cancer risk in age-adjusted and fully adjusted models

	Age-adjusted (CI)	Fully adjusted (CI)
Melanoma (HR)	$P_{\text{global}} = .004$	$P_{\text{global}} = .053$
Current vs never smoker	0.53 (0.31, 0.91)	0.55 (0.32, 0.94)
Past vs never smoker	1.20 (1.00, 1.42)	1.06 (0.88, 1.27)
NMSC (OR)	$P_{\text{global}} = .0002$	$P_{\text{global}} = .033$
Current vs never smoker	0.85 (0.76, 0.95)	0.86 (0.77, 0.96)
Past vs never smoker	1.05 (1.01, 1.1)	0.99 (0.95, 1.04)

Adjusted model is adjusted for age group, body mass index category, ethnicity/race, skin reaction to the sun, Langley exposure, education, physical activity, history of NMSC, history of malignant melanoma, summer sun exposure as a child, summer sun exposure currently, vitamin D, alcohol use, last medical visit within 1 year, any insurance, and income.

For melanoma, Cox proportional HR was used as the exact date of diagnosis was ascertained from medical records. For NMSC, subjects self-reported the diagnosis and thus we used logistic regression (OR).

CI, Confidence intervals; HR, hazard ratio; NMSC, nonmelanoma skin cancer; OR, odds ratio.