

## Short Communication

## Lower Skin Cancer Risk in Women with Higher Body Mass Index: The Women's Health Initiative Observational Study

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## Abstract

The unclear relationship of obesity to incident melanoma and nonmelanoma skin cancer (NMSC) risks was evaluated in the large, geographically diverse longitudinal, prospective Women's Health Initiative (WHI) observational study. Risks of melanoma and NMSC in normal weight women were compared with risks in overweight [body mass index (BMI) = 25–29.0 kg/m<sup>2</sup>] and obese (BMI ≥ 30 kg/m<sup>2</sup>) women, using Cox proportional hazards models for melanoma and logistic regression for NMSC. Over a mean 9.4 years of follow-up, there were 386 melanoma and 9,870 NMSC cases. Risk of melanoma did not differ across weight categories ( $P = 0.86$ ), whereas in fully adjusted models, NMSC risk was lower in overweight [OR, 0.93; 95% confidence interval (CI), 0.89–0.99] and obese (OR, 0.85; 95% CI, 0.80–0.91) women ( $P < 0.001$ ). Excess body weight was not associated with melanoma risk in postmenopausal women but was inversely associated with NMSC risk, possibly due to lower sun exposure in overweight and obese women. This supports previous work demonstrating the relationship between excess body weight and skin cancer risk. *Cancer Epidemiol Biomarkers Prev*; 22(12); 2412–5. ©2013 AACR.

## Introduction

Rates of skin cancer, the most common malignancy in the United States, affecting more than 3.5 million Americans each year, are increasing for both melanoma and nonmelanoma skin cancer (NMSC; ref. 1). Although obesity is linked to increased risks of colon, breast, endometrial, and ovarian cancers (2), its relationship to skin cancer is unclear. The Nurses' Health Study and Health Professionals Follow-up Study reported a lower NMSC risk in obese patients, but no association between body mass index (BMI) and melanoma (3). In a 2-year randomized low-fat diet trial, subjects who reduced their BMI also reduced their risk of NMSC (4). The longitudinal, prospective Women's Health Initiative (WHI) observational study provided an opportunity to investigate relationships of body weight status to melanoma and NMSC risks, taking into account key sunlight exposure variables, the major etiologic factors in skin cancer development (1).

## Materials and Methods

Postmenopausal women, ages 50 to 79 years, enrolled in the WHI observational study at 40 U.S. clinical centers from 1994 to 1998 ( $N = 93,676$ ), completed baseline questionnaires on key demographic and lifestyle variables (5). Because the majority of skin cancers occur in Caucasians and other ethnic groups did not demonstrate significant numbers of cases (1), analyses were restricted to White women ( $N = 78,016$ ) who were not underweight (BMI not less than 18.5;  $N = 76,208$ ) and had completed a sun exposure questionnaire at year 4 ( $N = 75,842$ ). Our final model used data from 61,657 subjects who had complete information on all variables included in the scientific model. Self-reported cases of melanoma and NMSC (representing both basal and squamous cell variants) were ascertained annually by questionnaire and melanoma cases were physician adjudicated, using medical records. Risks of melanoma and NMSC in normal weight women (BMI = 18.5–24.9 kg/m<sup>2</sup>) were compared with risks in overweight (BMI = 25–29.0 kg/m<sup>2</sup>) and obese (BMI ≥ 30 kg/m<sup>2</sup>) women, using Cox proportional hazards models for melanoma and logistic regression for NMSC (ODs with 95% confidence interval, CI), with subsequent adjustments for known baseline risk factors, for example, age, skin type (burn or tan), childhood summer sun exposure, baseline summer and ambient sun exposure (as Langley's at each clinical center across varying residential latitudes), smoking status, education, time walking outdoors per week, and self-reported history of skin or other cancer (see Table 1). Date of melanoma diagnosis was available from medical records, thus allowing for time to event methods (Cox) for melanoma analysis. For NMSC,

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**Table 1.** Baseline demographics among BMI groups of White women in the WHI observational study

Covariate	Normal (18.5–24.9 kg/m <sup>2</sup> )	Overweight (25–29.9 kg/m <sup>2</sup> )	Obese (30+ kg/m <sup>2</sup> )	Total
BMI (n, %)	26,396 (42.8)	21,208 (34.4)	14,053 (22.8)	61,657 (100)
Age group at baseline (n, %)				<i>P</i> < 0.0001
50–59	8,845 (33.5)	6,150 (29.0)	4,471 (31.8)	19,466
60–69	11,477 (43.5)	9,724 (45.9)	6,625 (47.1)	27,826
70–79+	6,074 (23.0)	5,334 (25.1)	2,957 (21.1)	14,365
Education (n, %)				<i>P</i> < 0.0001
Less than high school diploma or GED	6,141 (23.2)	6,145 (29.0)	5,072 (36.1)	17,358
Some school after high school diploma	6,807 (25.8)	5,936 (28.0)	4,089 (29.1)	16,832
College degree or higher	13,448 (51.0)	9,127 (43.0)	4,892 (34.8)	27,467
Times walked outside				<i>P</i> < 0.0001
Never	2,884 (10.9)	2,858 (13.5)	3,009 (21.4)	8,751
1–3×/mo	3,137 (11.9)	2,969 (14.0)	2,535 (18.0)	8,641
1–3×/wk	10,082 (38.2)	8,452 (39.8)	5,404 (38.5)	23,938
4–7+ /wk	10,293 (39.0)	6,929 (32.7)	3,105 (22.1)	20,327
Geographic sun exposure (Langleys)				<i>P</i> < 0.0001
300–325	7,887 (29.9)	7,007 (33.0)	4,944 (35.2)	19,838
350	5,154 (19.5)	4,612 (21.7)	3,313 (23.6)	13,079
375–380	3,399 (12.9)	2,203 (10.4)	1,333 (9.5)	6,935
400–430	4,427 (16.7)	3,344 (15.8)	2,037 (14.5)	9,808
475–500	5,529 (21.0)	4,042 (19.1)	2,426 (17.2)	11,997
NMSC at baseline				<i>P</i> < 0.0001
No	23,665 (89.7)	19,333 (91.2)	12,979 (92.4)	55,977
Yes	2,731 (10.3)	1,875 (8.8)	1,074 (7.6)	5,680
Melanoma at baseline				<i>P</i> = 0.021
No	26,120 (99.0)	20,934 (98.7)	13,872 (98.7)	60,926
Yes	276 (1.0)	274 (1.3)	181 (1.3)	731
Smoking status				<i>P</i> < 0.0001
Never smoked	13,326 (50.5)	10,520 (49.6)	6,996 (49.8)	30,842
Past smoker	11,431 (43.3)	9,605 (45.3)	6,451 (45.9)	27,487
Current smoker	1,639 (6.2)	1,083 (5.1)	606 (4.3)	3,328
Hormone therapy use				<i>P</i> < 0.0001
Never used	8,769 (33.2)	8,020 (37.8)	6,329 (45.1)	23,118
Past user	3,713 (14.1)	3,205 (15.1)	2,126 (15.1)	9,044
Current user	13,914 (52.7)	9,983 (47.1)	5,598 (39.8)	29,495
Skin reaction to the sun				<i>P</i> < 0.0001
Does not burn	9,601 (36.4)	7,654 (36.1)	4,753 (33.8)	22,008
Burns and then tans	14,212 (53.8)	11,004 (51.9)	7,310 (52.0)	32,526
Burns and does not tan	2,583 (9.8)	2,550 (12.0)	1,990 (14.2)	7,123
Time spent outdoors in summer as a child				<i>P</i> < 0.0001
Less than 30 minutes	609 (2.3)	440 (2.1)	322 (2.3)	1,371
30 minutes to 2 hours	7,282 (27.6)	5,419 (25.6)	3,194 (22.7)	15,895
More than 2 hours	18,505 (70.2)	15,349 (72.4)	10,537 (75.0)	44,391
Time spent outdoors in summer now				<i>P</i> < 0.0001
Less than 30 minutes	7,063 (26.7)	6,359 (30.0)	5,336 (38.0)	18,758
30 minutes to 2 hours	13,705 (51.9)	10,705 (50.5)	6,532 (46.5)	30,942
More than 2 hours	5,628 (21.4)	4,144 (19.5)	2,185 (15.5)	11,957
Usually use sunscreen outside				<i>P</i> < 0.0001
No	10,841 (41.1)	9,953 (46.9)	7,765 (55.3)	28,559
Yes	15,555 (58.9)	11,255 (53.1)	6,288 (44.7)	33,098

NOTE: Only those participants who were in the observational study of the WHI, reported their ethnicity as White, and were not missing any variables in the scientific model were included (there were 78,016 White women who were eligible). Outcomes are recorded from the start of the study period and participants are censored at death, last study visit, or 10 years from the start of the study period, whichever came first. Outcome events are recorded through August 2006.

**Table 2.** Age-adjusted and multivariate models for melanoma and NMSC

	Melanoma HR (95% CI)			NMSC OR (95% CI)		
	Cases (N, %)	Age-adjusted model	Adjusted model <sup>a</sup>	Cases (N, %)	Age-adjusted model	Adjusted model <sup>a</sup>
Normal (N = 26,396)	175 (0.66%)	1.0 (ref.)	1.0 (ref.)	4,683 (17.6%)	1.0 (ref.)	1.0 (ref.)
Overweight (N = 21,208)	137 (0.65%)	0.98 (0.78–1.22)	0.98 (0.74–1.29)	3,358 (15.8%)	0.87 (0.83–0.91)	0.93 (0.89–0.99)
Obese (N = 14,053)	74 (0.53%)	0.80 (0.61–1.05)	1.10 (0.95–1.28)	1,874 (13.3%)	0.73 (0.69–0.78)	0.86 (0.80–0.91)

<sup>a</sup>Adjusted for age, education, smoking, skin type, sun exposure, previous history of skin cancer, hormone therapy use, and sunscreen use.

participants reported this outcome yearly and this was not medical record adjudicated, thus only logistic regression could be performed.

## Results

Small, but statistically significant, differences in baseline characteristics were found among the 3 BMI groups (Table 1), including prior skin cancer and sun exposure, the most important predictors of skin cancer risk (1). Compared with the normal weight group, overweight and obese women reported less sun exposure (Table 1), based on average time walking outside ( $P < 0.001$ ), current sun exposure ( $P < 0.001$ ), and likelihood of living in areas of high geographic UV exposure ( $P < 0.0001$ ).

## Melanoma

Of note, 386 incident melanoma cases were reported (Table 2): 175 cases (0.66%) occurring in the normal weight group, 137 (0.65%) in the overweight group, and 74 (0.53%) in the obese group. Melanoma risk did not vary by weight category in either unadjusted or fully adjusted models ( $P = 0.86$ ). Relative to normal weight, HRs for overweight and obese women were 0.98 (95% CI, 0.74–1.29) and 1.10 (95% CI, 0.95–1.28), respectively (Table 2). Excluding women with prior history of skin cancer ( $N = 7,000$ ) did not change the result ( $P = 0.8$ ).

## Nonmelanoma skin cancer

A total of 9,870 NMSC cases were reported (Table 2) as follows: normal weight, 1,874 cases (17.6%); overweight, 3,358 (15.8%); and obese, 4,638 (13.3%), with a significant difference in risk among weight groups in both unadjusted and fully adjusted models ( $P < 0.0001$ ). Relative to normal weight, ORs for overweight and obese women were 0.93 (95% CI, 0.86–0.99) and 0.86 (95% CI, 0.80–0.91), respectively (Table 2). This relationship persisted even when participants with a history of skin cancer were excluded.

## Discussion

Excess body weight was not associated with melanoma risk in White postmenopausal women in the WHI cohort

over 9 years of follow-up, whereas it was significantly associated with NMSC risk. Specifically, overweight and obese women had a lower risk of NMSC than normal weight women. Overweight and obese women also reported less baseline sun exposure and it is conceivable that the lower NMSC risk was due to less sun exposure. Obese individuals have been shown to be less physically active and have less sun exposure at least in part because of being outdoors less frequently (3, 6). Pothiwala and colleagues demonstrated risk of NMSC, for which UV radiation has been shown to be most important, to be reduced to a greater extent in obese individuals (3). This supports the notion of diminished sun exposure for obese individuals, and could explain the decreased risk of NMSC seen in the WHI cohort. In contrast, melanoma risk is less well correlated with sun exposure (1). Of interest, this is in contrast with work demonstrating obese mice to have an increased (not decreased) susceptibility to skin cancer (7).

One of the strengths of the current analysis is the ability to adjust for sun exposure across a large, geographically diverse cohort over 9.4 years of follow-up. Despite adjustment for the major risk factor for skin cancer, i.e., sun exposure, it is possible that residual confounding arising from error in the self-reporting of this measure (8) may underlie the difference in NMSC risk by weight status.

Although there is a biologic mechanism between excess fat and skin cancer via oxidative DNA damage and intake of fatty foods (2), we did not observe a relationship between obesity and skin cancer risk in postmenopausal women. This confirms the prior work of Pothiwala and colleagues (3) and supports their finding that obesity may be a surrogate for lifetime sun exposure, resulting in lower rates of NMSC in overweight and obese women who receive less sun exposure.

## Disclosure of Potential Conflicts of Interest

J.Y. Tang is a consultant/advisory board member of Genentech. No potential conflicts of interest were disclosed by the other authors.

## Authors' Contributions

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