Height, nevus count, and risk of cutaneous malignant melanoma: Results from 2 large cohorts of US women

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Background: Taller individuals are at higher risk of melanoma.

Objective: To prospectively investigate the association of height with nevus count and melanoma and estimate the proportion of height-melanoma association explained by nevus count among white participants from the Nurses' Health Study (NHS) and Nurses' Health Study 2 (NHS2).

Methods: We used Cox proportional hazards regression and multinomial logistic regression for data analyses, with adjustment of potential confounders in the multivariate model.

Results: We included 82,468 and 106,069 women from NHS and NHS2, respectively. The hazard ratio was 1.21 (95% confidence interval [CI] 1.12-1.31) for the association between every 10-cm increase in height and melanoma. Compared with women with no nevi, the odds ratios (95% CIs) associated with a 10-cm increase in height were 1.35 (95% CI 1.23-1.48) in the NHS and 1.12 (95% CI 1.09-1.15) in the NHS2 for women with greater than or equal to 10 moles. The proportion of excess melanoma risk associated with each 10-cm increase in height explained by nevus count was 8.03% in the NHS and 10.22% in the NHS2.

Limitation: Self-reported height and nevus count. Mole counts were limited to 1 arm or both legs.

Conclusion: Nevus count is an important explanatory factor for the excess risk of melanoma among taller white women. (J Am Acad Dermatol 2020;83:1049-56.)

Key words: cutaneous melanoma; height; nevus count; prospective cohorts.

INTRODUCTION

Previous studies on adult height and risk of cutaneous malignant melanoma have generally reported a significant positive association; however, the magnitude of the association has varied among studies, with magnitude of hazard ratio ranging from 1.15 to 1.59 from prospective studies among women.[1-8] Such inconsistency is partly due to unmeasured confounding, given that many data sets lack information on potentially important confounders, such as human pigmentation, sun exposure history, and ancestry within the white population. Moreover, evidence on the association between height and nevus count, a well-known

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phenotype related to malignant melanoma, has been sparse, although a recent study among 2119 healthy UK women showed a positive correlation between height and number of nevi after adjustment for age, weight, twin relatedness, and leucocyte telomere length in a multivariate linear model (coefficient = 0.39; P = .003).[9] Thus, a comprehensive assessment on the association of height with nevus count and risk of melanoma is still lacking.

The UK study hypothesized that early-life growth, via higher stature, may influence risk of melanoma via increased nevus count.[9] However, to the best of our knowledge, no epidemiologic research has studied nevus count as an explanatory factor of the association between height and melanoma. Here, we used data from 2 large well-characterized prospective cohorts of US women to comprehensively examine the association of height with nevus count and melanoma risk. We also evaluated to what extent the observed association between height and melanoma was explained by nevus count.

CAPSULE SUMMARY

- Taller people are at higher risk of melanoma.
- In 2 large prospective cohorts of US women, height was positively associated with both nevus count and risk of melanoma. Nevus count explains approximately 8% to 10% of excess melanoma risk associated with a 10-cm increase in height.

METHODS

Study population

The Nurses' Health Study (NHS) is a prospective cohort study established in 1976 with 121,700 female US registered nurses who were then aged 30 to 55 years. The Nurses' Health Study 2 (NHS2) was established in 1989 with 116,429 female registered nurses aged 25 to 42 years and residing in the United States at enrollment. In both cohorts, participants completed and returned a mailed self-administered questionnaire about their medical histories and health-related exposures at baseline. Information regarding lifestyle and disease diagnoses was updated every 2 years, with a follow-up rate of greater than 90%. The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health, and those of participating registries as required.

Measurement of height, nevus count, and ascertainment of melanoma

Height was self-reported by participants at recruitment. In 1986, the NHS participants were asked to provide information on nevus count (>3 mm in diameter) from shoulder to wrist on the left arm by choosing from the following categories: none, 1 to 2, 3 to 5, 6 to 9, 10 to 14, 15 to 20, and 21 or greater. In 1989, the NHS2 participants reported numbers of nevi, without specification of size, on lower legs (knees to ankles, both legs), using the same categories. In both cohorts, participants reported new diagnoses of melanoma biennially. With permission, their medical reports were obtained and reviewed by physicians to confirm diagnoses. Only invasive melanomas were included in this analysis.

Measurement of covariates

Information on weight, smoking status, and menopausal status was first collected at baseline and then updated biennially. Body mass index was computed as weight in kilograms divided by the square of height in meters for each follow-up cycle. Food frequency questionnaires were initially collected in 1980 for the NHS and 1991 for the NHS2 and were generally updated every 4 years. Previous studies have demonstrated that food frequency questionnaires can validly assess dietary and alcohol intake.[10,11] Physical activity was first asked in 1986 in the NHS and in 1989 in the NHS2 and updated every 2 years thereafter. The reproducibility and validity of self-reported physical activity have been evaluated previously.[12]

Data on natural hair color, family history of melanoma, skin reaction after 2 hours of sun exposure as a child or adolescent, and number of severe sunburns were obtained from questionnaires in the NHS in the 1980s and in the NHS2 in the 1990s. Ambient erythemal ultraviolet radiation was estimated every 2 years since baseline with methods documented previously.[13] Participants reported new diagnoses of nonmelanoma skin cancer biennially. Medical reports were obtained and reviewed for squamous cell carcinoma but not for basal cell carcinoma. However, previous work supports the validity of self-reported basal cell carcinoma in our cohorts.[14,15] Ancestry within the white population was asked in the 1982 questionnaire in the NHS and the 1989 questionnaire in the NHS2. That information has been previously validated by comparing it with European ancestry estimated from genetic data.[16]

Abbreviations used:

CI: confidence interval
HR: hazard ratio
NHS: Nurses' Health Study
NHS2: Nurses' Health Study 2
OR: odds ratio

Statistical analysis

Height and melanoma. We excluded participants who did not report their date of birth. Participants with missing height or whose reported height was less than 120 cm or greater than 200 cm were excluded. Women who had cancers (except nonmelanoma skin cancer) at baseline were excluded, and those who reported any type of cancer (excluding nonmelanoma skin cancer) or died during follow-up were censored. We restricted the analysis among white participants because nonwhites are at low risk of developing skin cancer. We summarized number of participants excluded according to each criterion in Supplemental Table I (available via Mendeley at https://data.mendeley.com/datasets/4pt6b7fsr2/1). We followed participants for incident melanoma starting in 1976 in the NHS and 1989 in the NHS2. Age- and multivariable-adjusted Cox proportional hazards models were used to calculate hazard ratios and 95% confidence intervals (CIs) for the association between 10-cm increments in height and melanoma risk. Person-time was calculated for each participant from the date of baseline questionnaire return to the date of first report of melanoma, death, or the end of follow-up (June 2012 for the NHS and June 2013 for the NHS2), whichever came first. We evaluated the age-adjusted association of each candidate covariate with melanoma risk and height (Supplemental Table II). Only covariates significantly associated with both height and melanoma risk were considered as confounding factors. As a result, all covariates, except smoking status, body mass index, and menopausal status/postmenopausal hormone use, were included in the multivariable-adjusted Cox model. Multiplicative interactions between height and other covariates were tested with the likelihood ratio test comparing a main-effect-only model versus a model with the product term. All covariates in the full model were considered and sequentially tested for interaction 1 at a time. We tested heterogeneity of the results from the 2 cohorts with the Q statistic and conducted a fixed-effect inverse variance-weighted meta-analysis if no significant difference was detected.[17,18]

Height and nevus count. We further excluded women who did not report number of nevi from the analysis in which nevus count was the outcome of interest. Melanoma cases diagnosed before the year when the mole count question was asked (1986 in the NHS and 1989 in the NHS2) were excluded. We calculated odds ratios and 95% CIs for the associations between height (per 10-cm increase) and nevus count (4-level categoric variable: none as reference level, 1-2, 3-9, and ≥10) by using multinomial logistic regression models adjusting for baseline covariates status. All candidate covariates were included in the multivariable-adjusted model because they are significantly associated with both height (Supplemental Table II) and nevus count (significant Pearson correlations; data not shown). Heterogeneity of results was evaluated with the Q statistic as well.

Nevus count as an explanatory factor. The proportion of height-melanoma association that can be attributable to nevus count was assessed by calculating the percentage change in the β coefficient for height between Cox models adjusted for versus not adjusted for nevus count.[19,20] For this analysis, we set the year when nevus count was measured as baseline in the Cox models for melanoma risk (ie, 1986 in the NHS and 1989 in the NHS2).

All statistical analyses were performed with SAS (version 9.4; SAS Institute Inc., Cary, NC). We considered 2-sided $P < .05$ to be statistically significant.

RESULTS

Taller women tended to be younger, drank more alcohol, exercised more, and were more likely to be current smokers. Higher quartiles of height were more likely to be of Scandinavian ethnicity and to have a family history of melanoma, red or blond hair, presence of limb moles, and painful burn or blister skin reaction after prolonged sun exposure as a child or adolescent. These trends were consistent between the 2 cohorts. In the NHS, the percentage of current hormone replacement therapy users was higher among taller women (Table I).

Height and melanoma. We included 82,468 and 106,069 women from the NHS and NHS2, respectively. During 4,857,712 person-years of follow-up, we documented 1,543 incident melanoma cases (943 in the NHS and 600 in the NHS2). Height was significantly positively associated with risk of melanoma in both cohorts (Table II). In the multivariable-adjusted model, the combined hazard ratio from fixed-effect meta-analysis was 1.21

Table I. Baseline characteristics according to quartiles of height in the Nurses' Health Study (1976) and Nurses' Health Study 2 (1989)

	NHS Quartile (n = 82,468)				NHS2 Quartile (n = 106,069)			
Characteristics	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
Age,* mean (SD), y	42.5 (7.3)	42.2 (7.3)	41.9 (7.1)	41.4 (7.0)	36.1 (4.6)	36.0 (4.6)	36.0 (4.7)	35.7 (4.7)
Height, mean (SD), cm	155.70 (2.45)	161.51 (1.25)	166.37 (1.27)	172.52 (3.03)	157.19 (3.32)	162.56 (0)	166.42 (1.27)	173.05 (3.29)
Self-reported white ancestry, %								
Southern European/Mediterranean	27.4	22.2	19.9	16.9	23.4	19.8	18.3	16.5
Scandinavian	5.6	7.6	8.8	10.8	6.1	7.6	8.4	10.6
Other white	67.0	70.2	71.4	72.2	70.5	72.6	73.3	72.9
Family history of melanoma, %	7.9	8.1	8.3	8.7	13.9	14.3	14.7	15.4
Red/blonde hair, %	14.2	15.5	16.4	18.1	18.5	20.3	20.9	22.4
Limb with moles,† %	35.0	37.2	37.9	40.2	49.1	50.4	51.1	51.9
Painful burn/blisters reaction as a child/ adolescent, %	14.5	14.8	14.9	16.2	18.0	18.3	18.3	19.2
No. of blistering sunburns ≥5, %	6.8	7.7	7.7	8.6	8.9	10.1	10.5	11.4
Current smoking, %	31.3	31.1	31.5	33.1	13.8	12.9	13.0	13.9
Alcohol intake, mean (SD), g/d	5.9 (10.3)	6.5 (10.7)	6.9 (11.1)	7.3 (11.5)	2.9 (5.9)	3.1 (6.2)	3.3 (6.2)	3.4 (6.4)
Body mass index, mean (SD), kg/m^2	24.0 (4.2)	23.8 (4.1)	23.5 (4.0)	23.4 (3.9)	24.4 (5.1)	24.2 (5.1)	24.0 (5.1)	23.8 (5.0)
Physical activity level, mean (SD), metabolic equivalents h/wk	13.9 (19.2)	13.8 (20.1)	14.3 (20.3)	14.2 (20.1)	24.2 (35.9)	24.6 (36.4)	24.3 (35.1)	26.1 (38.1)
Annual ambient erythemal ultraviolet radiation, mean (SD), mW/m^2	181.7 (23.2)	182.7 (24.1)	183.4 (24.5)	184.6 (25.3)	169.7 (36.0)	171.3 (36.1)	172.4 (37.2)	174.1 (37.9)
Menopausal status/HRT use, %								
Premenopause	82.0	82.0	82.0	82.0	97.7	97.9	97.8	97.8
Never	8.2	8.2	8.2	7.9	0.1	0.1	0.1	0.1
Current	6.4	6.5	6.6	6.8	0.2	0.1	0.1	0.2
Past	3.5	3.3	3.2	3.3	2.1	1.8	2.0	1.9

Values are means (SD) or percentages and are standardized to the age distribution of the study populations. Values of multilevel categoric variables may not sum to 100% because of rounding. *HRT*, Hormone replacement therapy; *NHS*, Nurses' Health Study; *NHS2*, Nurses' Health Study 2; *SD*, standard deviation.

*Value is not age adjusted.

†NHS participants were asked to provide information on nevus count (>3 mm in diameter) from shoulder to wrist on the left arm. NHS2 participants reported numbers of nevi, without specification of size, from knees to ankles on both lower legs.

Table II. Hazard ratios and 95% confidence intervals for the associations of height (per 10-cm increase) with melanoma risk in the Nurses' Health Study (1976-2012), Nurses' Health Study 2 (1989-2013), and meta-analysis

				Age adjusted		Multivariable adjusted*	
	Person-years	No. of subjects	No. of cases	HR (95% CI)	*P* value	HR (95% CI)	*P* value
NHS	2,612,562	82,468	943	1.33 (1.20−1.48)	<.001	1.24 (1.11−1.37)	<.001
NHS2	2,245,150	106,069	600	1.27 (1.13−1.44)	<.001	1.18 (1.04−1.33)	.009
Meta-analysis†	4,857,712	188,537	1,543	1.31 (1.21−1.41)	<.001	1.21 (1.12−1.31)	<.001
P for heterogeneity†				.57		.56	

CI, Confidence interval; *HR*, hazard ratio; *NHS*, Nurses' Health Study; *NHS2*, Nurses' Health Study 2.
*Adjusted for age, alcohol intake (none and <5.0, 5.0-9.9, 10.0-19.9, or ≥20.0 g/day), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 metabolic equivalent hours/week), natural hair color (red, blonde, light brown, dark brown, or black), childhood/adolescent sunburn reaction (none or some redness, burn, or painful burn or blisters), family history of melanoma (yes or no), number of severe sunburns during lifetime (never, 1-2 times, 3-5 times, or ≥6 times), personal history of nonmelanoma skin cancer (yes or no), annual ambient erythemal ultraviolet radiation (in tertiles), self-reported white ancestry (Southern European/Mediterranean, Scandinavian, or other white), and mole count (none, 1-2, 3-9, or ≥10). We used the most updated information for time-varying covariates before each follow-up interval to take into account potential changes during follow-up. Missing data during any follow-up interval were coded as a missing indicator category for categoric covariates and with carried-forward values for continuous covariates.
†Fixed-effect meta-analysis was performed to combine results from the NHS and NHS2 because no significant heterogeneity was found.

(95% CI 1.12-1.31) for the association between each 10-cm increase in height and risk of invasive melanoma adjusted for all potential confounders (*P* for heterogeneity = .56). Moreover, we found no significant interactions between height and other covariates on melanoma risk in the multivariable-adjusted model (data not shown).

Height and nevus count. A total of 165,200 women (62,455 in the NHS and 102,745 in the NHS2) were eligible for this analysis. Taller participants had significantly more nevi on limbs (Table III). We did not combine results from the 2 cohorts because of significant heterogeneity. In the NHS, compared with women with no moles, the multivariable-adjusted odds ratios associated with a 10-cm increase in height were 1.08 (95% CI 1.04-1.11) for women with 1 to 2 moles, 1.20 (95% CI 1.15-1.25) for women with 3 to 9 moles, and 1.35 (95% CI 1.23-1.48) for women with greater than or equal to 10 moles, whereas in the NHS2, the multivariable-adjusted odds ratios were 1.03 (95% CI 1.00-1.05), 1.03 (95% CI 1.00-1.06), and 1.12 (95% CI 1.09-1.15), respectively.

Nevus count as an explanatory factor. In the NHS, 9.44% and 8.03% excess melanoma risk associated with each 10-cm increase in height was found to be explained by nevus count in age- and multivariable-adjusted models, respectively. In the NHS2, the age- and multivariable-adjusted explanatory proportions were estimated to be 10.47% and 10.22%, respectively (Table IV).

DISCUSSION

Height reflects a variety of environmental and genetic factors that may influence the risk of melanoma. In the present analysis, covariates adjusted in the multivariable model are unlikely to explain the observed positive association. One possible mechanism is that taller people may have a larger skin surface area, which means that more cells are at risk of malignant transformation.[21] Other postulated explanations focus on the link between height and certain early-life exposures such as nutritional status, stress, and severe disease during childhood.[22] Furthermore, melanoma is more common among people of higher socioeconomic status,[23] who also tend to have taller stature. Unfortunately, we were unable to investigate the role of body surface area, childhood exposures, or socioeconomic status because of the unavailability of relevant data.

Our finding that height is positively associated with nevus count is consistent with results from a previous study among 2119 UK female twins.[9] The researchers observed a significant positive association between height and nevus count, and hypothesized that such a link may be explained by telomere biology. Longer telomere is an important biomarker of reduced senescence in the melanocytic system, and it has been associated with elevated nevus count, larger nevus size, and increased risk of melanoma.[24,25] Telomere length has also been related to growth in early life, especially in female individuals.[9] However, the significant association between height and nevus count persisted after further adjustment for leukocyte telomere length in the UK study. In addition, controlling for environmental factors measured in later life, such as smoking status, alcohol intake, physical activity, postmenopausal hormone use, number of severe sunburns, and ultraviolet radiation, did not materially change the results of the current analysis. With evidence from the UK

Table III. Odds ratios and 95% confidence intervals for the associations between height (per 10-cm increase) and mole count with multinomial logistic regression analyses

	Mole count on limbs*						
	None	1–2		3–9		≥10	
Models		OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
NHS							
No. of participants	39,015	15,319		6,871		1,250	
Age adjusted	Reference	1.08 (1.05–1.12)	<.001	1.20 (1.16–1.26)	<.001	1.35 (1.23–1.48)	<.001
Multivariable adjusted†	Reference	1.08 (1.04–1.11)	<.001	1.20 (1.15–1.25)	<.001	1.35 (1.23–1.48)	<.001
NHS2							
No. of participants	50,727	19,427		17,515		15,076	
Age adjusted	Reference	1.04 (1.01–1.07)	.003	1.05 (1.03–1.08)	<.001	1.16 (1.13–1.19)	<.001
Multivariable adjusted†	Reference	1.03 (1.00–1.05)	.03	1.03 (1.00–1.06)	.04	1.12 (1.09–1.15)	<.001

CI, Confidence interval; *NHS*, Nurses' Health Study; *NHS2*, Nurses' Health Study 2; *OR*, odds ratio.

*Number of nevi on the left arm from shoulder to wrist in the NHS, and number of nevi on both lower legs from knees to ankles in the NHS2. We did not combine results from the 2 cohorts because of significant heterogeneity (*P* for heterogeneity <.05).

†Adjusted for age, smoking status (never, past, current, and 1-14, 15-24, or ≥25 cigarettes/day), alcohol intake (none or <5.0, 5.0-9.9, 10.0-19.9, or ≥20.0 g/day), body mass index (<25.0, 25.0-29.9, 30.0-34.9, or ≥35.0 kg/m^2), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 metabolic equivalent hours/week), menopausal status/postmenopausal hormone use (premenopausal or hormones never use, past use, or current use), natural hair color (red, blonde, light brown, dark brown, or black), childhood/adolescent sunburn reaction (none or some redness, burn, or painful burn or blisters), family history of melanoma (yes or no), number of severe sunburns during lifetime (never, 1-2 times, 3-5 times, or ≥6 times), personal history of nonmelanoma skin cancer (yes or no), annual ambient erythemal ultraviolet radiation (in tertiles), and self-reported white ancestry (Southern European/Mediterranean, Scandinavian, or other white). Missing indicators were created for categoric covariates.

Table IV. Proportion of association between height (per 10-cm increase) and risk of melanoma explained by nevus count in the Nurses' Health Study (1986-2012) and Nurses' Health Study 2 (1989-2013)

	NHS	NHS2
No. of melanoma cases	788	600
Person-years	1,790,900	2,245,150
Age adjusted		
Model 1, HR (95% CI)*	1.28 (1.14–1.43)	1.27 (1.13–1.44)
Model 2, HR (95% CI)*	1.25 (1.12–1.40)	1.24 (1.10–1.40)
Model 1, β coefficient for height*	0.2479	0.2397
Model 2, β coefficient for height*	0.2245	0.2146
Proportion explained by mole count, %†	9.44	10.47
Multivariable adjusted		
Model 3, HR (95% CI)*	1.21 (1.08–1.36)	1.20 (1.06–1.36)
Model 4, HR and 95% CI*	1.19 (1.06–1.34)	1.18 (1.04–1.33)
Model 3, β coefficient for height*	0.1919	0.1820
Model 4, β coefficient for height*	0.1765	0.1634
Proportion explained by mole count, %‡	8.03	10.22

We used the most updated information for time-varying covariates before each follow-up interval to take into account potential changes during follow-up. Missing data during any follow-up interval were coded as a missing indicator category for categoric covariates and with carried-forward values for continuous covariates.

CI, Confidence interval; *HR*, hazard ratio; *NHS*, Nurses' Health Study; *NHS2*, Nurses' Health Study 2.

*Model 1: age-adjusted model. Model 2: adjusted for age and mole count (none, 1-2, 3-9, and ≥10). Model 3: adjusted for age, alcohol intake (none or <5.0, 5.0-9.9, 10.0-19.9, or ≥20.0 g/day), physical activity (<3.0, 3.0-8.9, 9.0-17.9, 18.0-26.9, or ≥27.0 metabolic equivalent hours/week), natural hair color (red, blonde, light brown, dark brown, or black), childhood/adolescent sunburn reaction (none or some redness, burn, or painful burn or blisters), family history of melanoma (yes or no), number of severe sunburns during lifetime (never, 1-2 times, 3-5 times, or ≥6 times), personal history of nonmelanoma skin cancer (yes or no), annual ambient erythemal ultraviolet radiation (in tertiles), and self-reported white ancestry (Southern European/Mediterranean, Scandinavian, or other white). Model 4: adjusted for covariates in model 3 and mole count (none, 1-2, 3-9, or ≥10).

†Proportion explained by mole count is assessed by calculating the percentage change in the β coefficient for height between models 1 and 2.

‡Proportion explained by mole count is assessed by calculating the percentage change in the β coefficient for height between models 3 and 4.

study and the current analysis taken together, it is possible that early-life exposures and nontelomere-related genetic factors are involved in the association between height and nevus count.

There is evidence that bone metabolism and the melanocytic system are related at the genetic level. In vertebrates, neural crest cells give rise to many different cell types, including osteoblasts and melanoblasts.[26] Some of the genes involved in melanocyte differentiation and invasion have been identified as associated with bone density by genetic association studies.[27-31] In a recent large genome-wide association study on height, many of the height-related genes were also found to be related to cancer pathways.[32] Mendelian randomization analyses demonstrated a potential causal relationship between adult height and risk of colorectal and lung cancer, which suggests that certain height-related genetic factors may also affect risk of cancers.[33] In sum, the connections observed among height, nevus count, and melanoma may be explained by a complex network of genes involved in embryogenesis, growth, and nevogenesis.

We performed additional analyses to estimate proportion of association between mole count and risk of melanoma explained by height (Supplemental Table III), although they were not the primary focus of this article. In multivariate models, height explains 1.37% and 0.60% of nevus count—melanoma association in the NHS and NHS2, respectively, which are much lower compared with the explanatory proportions of mole count in height-melanoma association. Such difference is likely due to the much stronger association between mole count and melanoma than that between height and melanoma. Another possibility is that height may have a stronger association with de novo melanoma than with nevus-associated melanoma, therefore accounting for only a small proportion in mole count—melanoma association. However, our data are insufficient to test this hypothesis.

Our study has several strengths. We used data from 2 large prospective cohorts with high rates of long-term follow-up. With detailed information on a wide variety of covariates, we were able to examine the associations between height and melanoma as well as mole count more thoroughly than what has previously been reported. We also acknowledge a few potential limitations. First, height and nevus count were self-reported in our cohorts. However, a previous study has shown high correlation between self-reported and technician-measured height within the NHS.[34] Studies also found substantial agreement between nevus self-counts and dermatologist counts.[35-37] In our cohorts, the ordinal variable of nevus count was a highly significant predictor of melanoma risk.[38] Genetic association studies using this variable identified previously reported nevus-related genes.[39,40] Second, we were unable to control all potential confounding variables. For example, data on socioeconomic status and exposures during childhood were not available. However, our participants were all nurses, which could minimize confounding by educational attainment and adult socioeconomic status. Third, the question on nevus count is different between the NHS and NHS2. To avoid the potential influence of this matter on the results, we first conducted cohort-specific analysis, and the results for the associations of height with nevus count as well as melanoma risk were consistent between the 2 cohorts. Finally, our study population consisted of only white female nurses, and thus results may not be generalizable. However, studies among this rather homogeneous group are likely to minimize confounding by socioeconomic status and differential access to health care and ensure high-quality returned data.

In conclusion, our study among white female nurses provides further evidence that increased height is associated with elevated risk of melanoma. Taller people tend to have more nevi on their limbs, and nevus count appeared to be a significant explanatory factor in the association between height and melanoma. Additional research involving a range of preadult exposures and genetic epidemiologic studies designed to estimate shared heritability and identify markers of pleiotropic effects may help clarify the underlying mechanisms.

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