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Male pattern baldness and risk of incident skin cancer in a cohort of men

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Abstract

We examined the association between male-pattern baldness and risk of incident skin cancer, including invasive melanoma, invasive squamous cell carcinoma (SCC), and basal cell carcinoma (BCC) in a prospective analysis, based on 36,032 participants from the Health Professionals' Follow-up Study. In 1992, participants reported their status of male-pattern baldness at age 45 years by choosing from five crown-view pictograms based on Norwood's classification. Diagnosis of skin cancers was reported biennially and information on melanoma and SCC was pathologically confirmed. We identified 327 melanoma cases, 1324 SCC cases, and 8438 BCC cases during the follow-up. Male-pattern baldness was not significantly associated with risk of incident melanoma, but was significantly associated with increased risk of SCC and BCC. The multivariate-adjusted hazard ratio (HR) (95% confidence interval, CI) for the highest category of baldness (frontal plus severe vertex baldness) was 1.33 (1.06–1.68) for SCC ($P_{trend}=0.001$) and 1.23 (1.12–1.35) for BCC ($P_{trend}<0.0001$), compared with no baldness. Analyses by body sites found significant associations between frontal plus moderate to severe vertex baldness and risk of melanoma (HR=1.83, 95% CI: 1.01–3.34) and SCC (HR=1.30, 95% CI: 1.02–1.66) at head and neck. The associations were particularly stronger for scalp melanoma (HR=7.15, 95% CI: 1.29–39.42) and scalp SCC (HR=7.09, 95% CI: 3.84–13.08), but not for non-scalp head and neck sites. Information on body sites was not available for BCC. In conclusion, male pattern baldness may be associated with increased risk of skin cancer, but the associations may only exist for those occurring at head and neck, particularly at scalp.

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Keywords

male pattern baldness; melanoma; squamous cell carcinoma; head and neck; scalp; basal cell carcinoma

Introduction

Male pattern baldness (also known as male androgenetic alopecia) is the most common cause of male hair loss, characterized by a progressive hair follicular miniaturization¹⁻³. Male pattern baldness is associated with higher levels of dihydrotestosterone and increased expression of androgen receptors⁴. The pathogenesis is generally considered as an androgen-mediated process in genetically susceptible individuals, and environmental and lifestyle risk factors are likely to be triggers³⁻⁷. Male pattern baldness has been associated with increased risk of prostate cancer^{8,9}.

A potential androgen basis of melanoma has been proposed to explain the differential gender distribution of melanoma^{10,11}, based on which we reported increased risk of melanoma but not keratinocyte carcinoma (KC, also known as non-melanoma skin cancer) associated with personal history of prostate cancer in the Health Professionals' Follow-up Study (HPFS)¹². Supporting the androgen basis, our group recently reported that women with a history of severe teenage acne had higher midlife plasma free testosterone levels and displayed increased risk of melanoma¹³. The potentially common androgen basis could suggest a possible link between male pattern baldness and risk of melanoma. If the association between male pattern baldness and risk of melanoma is true and if androgen basis is the major mechanism underlying the association, one would expect null or much weaker associations between male pattern baldness and KC to release the concern on the confounding by sun exposure and the effect of detection bias. In addition, previous studies on male pattern baldness and risk of skin cancer were sparse, with some clinical evidence reporting that skin cancer of the scalp occurs more frequently in balding men^{1,14}. Prior literatures have also proposed that the long-term protective role of hair cover may reduce UV exposure and may be associated with the higher incidence of head and neck melanomas in men than in women, as reviewed before¹⁵.

In our study, we examined the association between male pattern baldness at age 45 and risk of incident melanoma, squamous cell carcinoma (SCC), and basal cell carcinoma (BCC), the three predominant types of skin cancer, based on the HPFS. Here we report our findings, which showed that male pattern baldness was significantly associated with increased risk of both SCC and BCC, but was not significantly associated with risk of melanoma overall. Male pattern baldness was significantly associated with melanoma and SCC at head and neck only, particularly at scalp. Therefore, despite the long hypothesized androgen-related mechanism for melanoma development, our results suggest that the androgen basis might not be the major mechanism underlying the observed associations between male pattern baldness and skin cancer.

Methods

Study population

The HPFS began in 1986 when 51,529 US male health professionals aged 40–75 years, completed a baseline questionnaire on medical history and lifestyle practices. Health professionals are highly motivated and committed to participating in this long-term project and appreciate the accuracy of reports, with their knowledge as a quality assurance. Biennially, participants received a questionnaire and a response rate generally exceeding 90% has been achieved in the follow-up. The study was approved by the Human Research Committee of Harvard School of Public Health (Boston, MA). Participants' completion and return of the questionnaire was considered informed consent.

Assessment of main exposure

In the 1992 questionnaire, participants were asked about their balding status at age 45 years by choosing from five crown-view images based on the Norwood-Hamilton's classification of male-pattern baldness¹⁶. The five pictograms correspond to no baldness (Norwood's I), frontal baldness only (Norwood's II+III), frontal plus mild vertex baldness (Norwood's III vertex+IV), frontal plus moderate vertex baldness (Norwood's V+VI), and frontal plus severe vertex baldness (Norwood's VII).

Assessment of covariates

In the HPFS, information on smoking, body mass index (BMI), physical activity, and physical examination in the recent 2 years was available in the biennial questionnaire from 1986. Race/ethnicity was asked in 1986. Information on the number of moles with 3 mm diameter on arms was collected in 1987. Natural hair color at age 18 years was asked in 1988. Number of blistered sunburn throughout life and adolescent tendency to sunburn were asked in 1992. Sun-tanning ability was not asked in the cohort. Family history of melanoma in first-degree relatives was asked in 1990 and 1992. Information on outdoor sun exposure between 10 am and 3 pm in summer for high school/college, at age 25–35, 36–59, and 60 years was collected in 2008. Information on state of residence was updated biennially. According to the state of residence in each 2-year follow-up cycle, UV flux for a participant that could have received over a period of time was estimated by summing up the 6-month Robertson–Berger unit counts over the follow-up¹⁷, using the methods detailed previously¹⁸.

Assessment of outcome

Since 1986, participants have reported diagnoses of melanoma, SCC, BCC, and other cancers on biennial surveys. When a diagnosis was reported, the participant was entered a tracking system. Related medical records were requested with the participant's permission and reviewed by physicians blinded to exposure to confirm the diagnosis. For melanoma and SCC, we excluded self-reported cases that denied the diagnosis in the further follow-up or denied the permission to review their records, and only those pathologically confirmed invasive cases in the medical record review were documented as the outcome. For BCC, we did not seek to obtain the medical records for all, but previous studies have indicated a high validity of self-reports, with more than 90% confirmed by histopathology records^{19, 20}. We

have the information on body sites for melanoma and SCC but not for BCC. Information on diagnoses has been updated to 2010 for SCC and to 2012 for melanoma and BCC.

Statistical Analysis

As male pattern baldness was asked in 1992, we set 1992 as the study baseline. Among 40,041 participants who responded to question on balding status, we excluded participants reporting diagnosis of cancer (melanoma, SCC, BCC, or other non-skin cancers) at or before the 1992 questionnaire, a total of 36,032 participants remained for the analysis.

Person-years of follow-up were calculated from the date of the return of the 1992 questionnaire to the diagnosis date of melanoma, SCC, or BCC, death, last questionnaire response, or end of follow-up (Jan 2010 for SCC and Jan 2012 for melanoma and BCC), whichever came first. We calculated the hazard ratios (HRs) and 95% confidence intervals (CIs) for each category of male pattern baldness, compared with those with no baldness. The analyses were conducted using Cox proportional hazards analysis stratified by age and 2-year interval, adjusting *a priori* for BMI, smoking, physical activity, childhood reaction to sun, number of sunburns, mole count, hair color, family history of melanoma, average summer time sun exposures, and adult life UV flux (cumulative UV flux since cohort baseline). An indicator was created for the missing data of each covariate. These covariates were included in the multivariate-adjusted models because they have been previously associated with skin cancer in our cohorts. Information on the covariates was updated in each 2-year questionnaire cycle, whenever available. In a sensitivity analysis, we additionally adjusted for physical examination. In a secondary analysis, we performed a lag analysis in which skin cancer diagnosed during the first 2 years of follow-up were excluded. In another secondary analysis, all analyses were restricted to Caucasians, as the prevalence of male pattern baldness varies among different ethnic backgrounds²¹.

We examined the association between male pattern baldness and risk of site-specific melanoma [head and neck melanoma (HNM), other sun-exposed sites (upper limb, leg, or ankle), and less sun-exposed/sun-protected sites (all other sites)] and SCC (head and neck, other sun-exposed sites, and less sun-exposed/sun-protected sites). For head and neck melanoma and SCC, we further explored scalp and non-scalp cancers respectively. To examine whether sun exposure related variables could modify the associations, subgroup analyses by adult life UV flux (dichotomized by the median), hours of summer time sun exposure (dichotomized by the median), lifetime number of sunburns (dichotomized by the median), and melanoma subtypes [lentigo maligna melanoma (LMM) or non-LMM] were conducted. *P* values for heterogeneity for the associations across body sites (scalp, non-scalp head and neck sites, other sun-exposed sites, or sun less-exposed sites) were calculated by using *Q* statistics. For consideration of statistical power for site-specific analyses and other subgroup analyses, male pattern baldness was re-classified as three categories: no (Norwood's I), moderate (frontal only or plus mild vertex baldness, Norwood's II~IV), or severe baldness (frontal plus moderate to severe vertex baldness, Norwood's V~VII).

Analyses were carried out by using SAS (version 9.2; SAS Institute Inc, Cary, NC). All *P* values were 2-tailed with the significance level set at *P* < 0.05.

Results

Among 36,032 participants, 56.0% (20,173) reported hair loss with at least frontal male pattern baldness at age 45 years. 8.0% (2,871) had frontal plus moderate vertex baldness and 5.7% (2,056) had frontal plus severe vertex baldness. Baseline characteristics of the participants according to male pattern baldness are shown in Table 1. Men with more severe baldness tended to have lower annual UV flux at baseline.

We identified 327 cases of melanoma during 507,113 person-years' follow-up (1992–2012), 1,324 cases of SCC during 460,392 person-years (1992–2010), and 8,438 cases of BCC during 499,386 person-years (1992–2012). Male-pattern baldness was not significantly associated with risk of incident melanoma overall (Table 2). In contrast, each of the four categories of baldness was significantly associated with increased risk of both SCC and BCC. Compared with no baldness, the multivariate-adjusted HR (95% CI) associated with SCC was 1.22 (1.07–1.40) for frontal only, 1.22 (1.04–1.42) for frontal plus mild vertex, 1.23 (1.01–1.51) for frontal plus moderate vertex, and 1.33 (1.06–1.68) for frontal plus severe vertex baldness, compared with no baldness (P for trend=0.001) (Table 3). For BCC, the HR was 1.10 (1.04–1.16) for frontal only, 1.12 (1.06–1.19) for frontal plus mild vertex, 1.11 (1.03–1.20) for frontal plus moderate vertex, and 1.23 (1.12–1.35) for frontal plus severe vertex baldness (P for trend<0.0001) (Supplementary Table S1). The multivariate-adjusted analyses adjusting for average sun exposure, adult life UV flux and other variables reached similar HRs with the age-adjusted analyses (Table 2–3 and Supplementary Table S1).

We examined the association by skin cancer at different body sites and found that severe baldness (frontal plus moderate to severe vertex baldness) was associated with HNM (HR=1.83, 95% CI: 1.01–3.34). The association was particularly stronger for scalp melanoma (HR=7.15, 95% CI: 1.29–39.42), although our analysis was restricted by the extremely limited case numbers. For melanoma at other sun-exposed sites or sun-protected/sun less--exposed sites, we did not find significant associations. We observed significant heterogeneity for the associations with melanoma in different body sites (P for heterogeneity=0.049 for severe baldness). For SCC, the significant association with male pattern baldness was also found only for head and neck SCC (HR=1.30, 95% CI: 1.02–1.66 for frontal plus moderate to severe vertex baldness), particularly SCC at the scalp (HR=7.09, 95% CI: 3.84–13.08), but not for SCC at other sun-exposed sites or sun-exposed sites (Table 3). The associations were significantly heterogeneous across SCC body sites (P for heterogeneity<0.0001 for severe baldness). The multivariate-adjusted analyses yielded similar HRs with the age-adjusted analyses (Table 2–3).

Subgroup analyses found that the association between male pattern baldness and risk of incident HNM was significant among participants with adult life UV flux at or higher than the median (HR=2.39, 95% CI: 1.00–5.75), but was not among those with the lower adult life UV flux (HR=1.46, 95% CI: 0.63–3.39 for frontal plus moderate to severe vertex baldness). However, the CIs for the two HRs overlap each other and we did not find significant interaction between adult life UV flux and male pattern baldness (P for interaction=0.41, Supplementary Table S2). Subgroup analysis by summer time sun

exposure, lifetime number of sunburns, or LMM/non-LMM yielded similar findings among different strata. For SCC or BCC overall and SCC at different body sites, the subgroup analyses found similar associations with male pattern baldness across different strata (data not shown).

Lag analyses excluding the skin cancer cases in the first follow-up period, sensitivity analysis additionally adjusting for physical examination, or analyses restricting to Caucasians did not show material change of the associations.

Discussion

In our study, male-pattern baldness at age 45 was significantly associated with increased risk of both SCC and BCC. In contrast, male pattern baldness was not significantly associated with risk of melanoma overall, with even a lower effect estimate for melanoma than SCC and BCC. Male pattern baldness was positively associated with melanoma and SCC at head and neck only, particularly the scalp melanoma and SCC. To our knowledge, this is the first prospective study to report the associations between male pattern baldness and risk of incident skin cancer.

One rationale that we conduct our current study is the potentially common androgen basis of male pattern baldness and melanoma. It has been well known that female melanoma patients generally exhibit better prognosis than male patients²². In our prior study, a significant association between severe teenage acne and an increased risk of melanoma has been reported^{13, 23}. We proposed that a history of teenage acne may be an early-stage marker of high androgen levels, supported by the elevated midlife free testosterone levels¹³. In another study, we found a positive association between prostate cancer and risk of incident melanoma, with a significantly higher effect magnitude than the association with KC¹². However, in the current analysis, male pattern baldness at age 45 was significantly associated with increased risk of both SCC and BCC, but was not significantly associated with risk of melanoma overall, with even a lower effect estimate for melanoma. In addition, we observed similar HRs for HNM and head and neck SCC (P for heterogeneity=0.31), and similar HRs for scalp melanoma and scalp SCC (P for heterogeneity=0.99) associated with frontal plus moderate to severe vertex baldness. Because our findings do not comply fully with our initial hypothesis and expectations, androgen basis might not be the major mechanism underlying the observed associations between male pattern baldness and skin cancer. However, further studies are still required to explore the long hypothesized androgen basis of melanoma and to examine whether the role of androgen underlying melanoma pathophysiologic processes would be particularly stronger for melanoma at specific body sites.

Although prior studies on male pattern baldness and risk of skin cancer were sparse, there was anecdotal impression in clinics that balding may be a risk factor for both melanoma and KC in scalp compared with non-balding¹, with the perception of delayed detection due to concealment from hair coverage, as well as the protection against sun damage to scalp by hair coverage in non-balding men. Studies have also linked hair cover and hairstyle to anatomic distribution of melanoma¹⁵. One clinical cross-sectional study found a significant

association between male pattern baldness and both melanoma and KC of the scalp¹⁴. Our findings in a prospective study on male pattern baldness and risk of incident scalp melanoma and SCC corroborated prior clinical knowledge. As we do not have information on BCC body sites, it is unclear whether the association between baldness and BCC may also exist solely for head and neck BCC.

Clinically, compared with melanoma of other skin sites, HNM, particularly scalp melanoma, is more aggressive and have an overall poorer prognosis, which may be partly explained by a late diagnosis due to hidden by hair^{24–26}. Our findings may also be partly attributed to the timely diagnosis among balding men compared with non-balding men. The association of male pattern baldness with head and neck (scalp) melanoma and SCC could also be due to sun exposure, particularly if the melanomas were LMM type. In our study, the significant association for HNM existed only among those who exposed to higher adult life UV flux, an indicator for chronic sun exposure. However, the interaction analysis did not find significant interaction. In addition, subgroup analyses for melanoma by summer time sun exposure or number of sunburns, as well as subgroup analyses for scalp SCC generally reached similar associations across strata. Therefore, although differences in sun exposure may partly explain the results, the observed distinct incidence of head and neck melanoma (SCC) between balding and non-balding men may not be entirely explained by sun exposure. Whether the distinct patterns of sun exposure contributed to the association requires further studies to clarify.

It is biologically plausible that male pattern baldness may be a marker of other aberrations. Finding the common genetic polymorphisms for male pattern baldness and skin cancer may help provide important insights into the mechanisms. In prior studies, men with baldness have been associated with elevated levels of circulating insulin-like growth factor 1 (IGF-1)^{27, 28}. IGF-1 plays an important role in tumor maintenance and development due to its antiapoptotic and mitogenic effects, and the circulating concentrations of IGF-1 are positively associated with risk of common cancers⁹. Although the evidence for IGF-1 and KC has been sparse, IGF-1 may induce proliferation and migration of keratinocytes^{29, 30}. The role of IGF-1 in melanoma has been implicated in previous studies, which showed that IGF-1 enhances survival, migration, and growth of melanoma cells^{9, 31–33}. The mechanism by IGF-1 for our findings may be worth considering as well.

In our study, we comprehensively adjusted for the major lifestyle characteristics, pigmented traits, and other skin cancer risk factors, so the observed associations were less likely mediated by these confounders. Balding men did not have more physical examinations than non-balding men in our study (Table 1). The analyses adjusting for physical examination did not appreciably change the results. Therefore, physical examination may not be a major mediator for the observations. As balding men may use medications for hair restoration, it would be interesting to investigate whether the medications would be the underlying triggers for increased risk of skin cancer as well. However, we did not collect information on use of hair stimulating medicines.

Our study was strengthened by its prospective design, detailed information on potential confounders, updated assessment of skin cancer diagnosis, and information on the locations

of melanoma and SCC. The follow-up and response rate in the cohort has been very high (generally >90%), which releases the concern of selection bias as a result of participant dropout. We are aware of some limitations. First, male pattern baldness at age 45 years was collected in 1992, when participants were 45~83 years. With a single self-report, we were not able to examine the association for baldness at different ages or the progressive patterns as the main exposure. Recall bias may also be possible. Participants may have underreported the severity of baldness, which is known to have negative socio-psychological effects³⁴. However, as our study was based on a prospective cohort with skin cancer occurring after the assessment of baldness, any misclassification by the recall bias or underreport may tend to be non-differential between skin cancer cases and non-cases. The effect estimates may therefore have been conservative estimates of the associations. Second, a diagnosis of baldness may be associated with some aspects of lifestyle risk factors. An observational study cannot rule out the possibility of residual confounding by unmeasured or imperfectly measured confounders, such as the lifetime sun exposure and skin examination. Third, as the sites of BCC were not collected, we were not able to compare the effect magnitude between sites of melanoma and BCC. We also do not exclude the possibility of underreporting of BCC but any report bias may tend to be non-differential across the categories of baldness. Fourth, we only have a modest sample size for melanoma, which limited the statistical power and may particularly be a concern for the subgroup analyses by body sites and UV flux. We therefore re-categorized the baldness for the subgroup analyses. Although heterogeneity tests tend to be very conservative, we reported statistically-significant heterogeneity of the associations across body sites of melanoma and SCC. Considering the study hypothesis and findings, the current study was able to answer the research questions and support the final conclusions. Fifth, study participants were health professionals and most were Whites. The homogeneity has enhanced the quality of questionnaire response and minimized confounding from socioeconomic factors, but any extrapolation to the general population, should be approached with caution.

In conclusion, male pattern baldness was positively associated with increased risk of SCC and BCC, but was not significantly associated with increased risk of melanoma. The associations with melanoma and SCC were significant only for those occurring at head and neck, particularly the scalp cancer. Further studies are warranted to examine the associations specifically for BCC at different body sites and elucidate the mechanisms underlying the observed associations. Pending further replication with a large sample size, our findings hold clinical implications that male pattern baldness may contribute to the identification of those at high risk for skin cancer, which may inform clinical practice to address the queries and to pay special attention to head and neck (particularly scalp) skin cancers among balding men. Public messages are also warranted for balding men to protect the skin on their head from excessive sun exposure.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What's new

We conducted the first prospective analysis on male-pattern baldness and risk of incident skin cancer. Male-pattern baldness was significantly associated with increased risk of squamous cell carcinoma (SCC) and basal cell carcinoma, but was not significantly associated with melanoma overall. The associations with melanoma and SCC were significant only for those occurring at head and neck, particularly the scalp. Clinicians may pay special attention to head and neck (particularly scalp) skin cancers among balding men.

Table 1

Baseline characteristics of the study population according to male pattern baldness at age 45 years: Health Professionals' Follow-up Study¹

	No	Frontal only	Male-pattern baldness ²			<i>P</i> ³
			Frontal + mild vertex	Frontal + moderate vertex	Frontal + severe vertex	
n	n=15,859	n=9,127	n=6,119	n=2,871	n=2,056	
Age, mean (SD), year	59.1(9.5)	59.4(9.7)	58.6(9.5)	59.9(9.7)	59.4(9.9)	<0.0001
Ethnicity (Whites, %)	92.4	93.1	93.0	93.5	94.1	0.01
Body mass index, kg/m², mean (SD)	22.1(9.5)	22.0(9.5)	22.0(9.7)	22.2(9.8)	22.3(10.0)	0.55
Physical activity, metabolic equivalent hours/wk, mean (SD)	37.6(42.1)	36.6(40.5)	37.1(43.6)	36.9(43.0)	35.8(40.0)	0.21
Current smoking (%)	7.6	7.1	6.8	6.1	6.1	0.003
Family history of melanoma (%)	4.3	4.5	4.2	5.1	4.2	0.59
Burn or blistering skin reaction to the sun (%)	67.1	70.4	69.2	71.0	70.2	<0.0001
Natural red or blonde hair (%)	12.6	15.2	12.2	13.6	15.0	<0.0001
6 moles on an extremity, 3+ mm diameter (%)	5.3	5.2	5.6	4.8	5.1	0.90
History of 6 severe or blistering sunburns (%)	34.2	35.7	34.2	34.9	35.2	0.32
Annual UV flux (×10⁻⁴ RB count)	131.1(27.9)	130.5(27.7)	129.3(27.6)	129.1(27.5)	128.7(27.0)	<0.0001
Lifetime average summer time sun exposure 11 hrs/wk (%)	28.9	29.1	28.9	28.2	25.9	0.12
Physical examination in recent 2 years, %	80.1	80.4	81.8	81.0	81.6	0.04

¹ All values other than age were age-adjusted.

² Male pattern baldness based on the Norwood-Hamilton's scale: no baldness (Norwood's I), frontal baldness only (II-III), frontal plus mild vertex baldness (III vertex+IV), frontal plus moderate vertex baldness (V+VI), and frontal plus severe vertex baldness (VII).

³ *P* values were calculated by using one-way ANOVA (for continuous variables) or chi-square test (for categorical variables).

Table 2

HRs (95% CIs) for the association between male pattern baldness at age 45 and risk of incident melanoma (1992–2012)

	Male pattern baldness				P for trend
	No	Frontal only	Frontal + mild vertex	Frontal + moderate vertex	Frontal + severe vertex
Melanoma overall					
Person-years	225,322	127,354	86,625	40,018	27,795
Cases	141	83	57	25	21
Age-adjusted HR (95% CI)	1.00	1.02 (0.78–1.34)	1.06 (0.78–1.44)	0.96 (0.63–1.48)	1.19 (0.75–1.89)
Multivariate-adjusted HR ² (95% CI)	1.00	0.98 (0.75–1.29)	1.01 (0.74–1.38)	0.94 (0.61–1.44)	1.17 (0.74–1.85)
Melanoma by body site²					
Person-years	225,322		213,979		67,813
Head and neck					
Cases	30		41		17
Age-adjusted HR (95% CI)	1.00		1.45 (0.91–2.33)		1.84 (1.01–3.34)
Multivariate-adjusted HR ² (95% CI)	1.00		1.40 (0.87–2.25)		1.83 (1.01–3.34)
Scalp					
Cases	2		8		4
Age-adjusted HR (95% CI)	1.00		4.22 (0.89–19.90)		6.54 (1.20–35.74)
Multivariate-adjusted HR ² (95% CI)	1.00		4.58 (0.96–21.73)		7.15 (1.29–39.42)
Other head and neck sites					
Cases	28		33		13
Age-adjusted HR (95% CI)	1.00		1.25 (0.76–2.08)		1.50 (0.78–2.90)
Multivariate-adjusted HR ² (95% CI)	1.00		1.19 (0.72–1.98)		1.49 (0.77–2.89)
Sun-exposed sites other than head and neck					
Cases	24		24		7
Age-adjusted HR (95% CI)	1.00		1.05 (0.59–1.84)		0.95 (0.41–2.22)
Multivariate-adjusted HR ² (95% CI)	1.00		0.99 (0.56–1.74)		0.93 (0.40–2.18)
Sun less-exposed sites					
Cases	74		58		17
Age-adjusted HR (95% CI)	1.00		0.81 (0.57–1.14)		0.74 (0.44–1.26)
					0.17

Male pattern baldness					P for trend
Melanoma overall	No	Frontal only	Frontal + mild vertex	Frontal + moderate vertex	
Multivariate-adjusted HR ² (95% CI)	1.00	0.78 (0.55–1.10)		0.73 (0.43–1.23)	0.10

¹ Multivariate-adjusted analyses were performed adjusting for age (continuous variable), race/ethnicity (Caucasian, Asian, African American, or others), body mass index (<18.5, 18.5–24.9, 25–29.9, 30–34.9, or ≥35 kg/m²), smoking (never, past, or current smokers), physical activity (in quintiles, metabolic equivalent hours/wk), childhood reaction to sun (tan without burn, burn, or painful burn/blisters), times of sunburns (0, 1–2, 3–5, or ≥6), mole count (0, 1–2, 3–5, or ≥6), hair color (red, blonde, light brown, or dark brown/black), family history of melanoma (yes or no), average sun exposures of high school, age 25–35, age 36–59, and age ≥60 (<1, 2–5, 6–10, or ≥11 hours), adult life UV flux (in quintiles). An indicator variable was created for the missing value of each covariate.

² For the analysis by body sites, male pattern baldness was re-classified as three categories: no, moderate (frontal only or with mild vertex baldness), or severe baldness (frontal plus moderate to severe vertex baldness), due to power consideration.

Table 3

HRs (95% CIs) for the association between male pattern baldness at age 45 and risk of incident squamous cell carcinoma (1992–2010)

	Male pattern baldness				P for trend
	No	Frontal only	Frontal + mild vertex	Frontal + moderate vertex	Frontal + severe vertex
Squamous cell carcinoma overall					
Person-years	204,216	115,875	78,533	36,449	25,319
Cases	517	369	237	118	83
Age-adjusted HR (95% CI)	1.00	1.26 (1.10–1.44)	1.22 (1.05–1.43)	1.26 (1.03–1.54)	1.33 (1.05–1.68)
Multivariate-adjusted HR ¹ (95% CI)	1.00	1.22 (1.07–1.40)	1.22 (1.04–1.42)	1.23 (1.01–1.51)	1.33 (1.06–1.68)
Squamous cell carcinoma by body site²					
Person-years	204,216		194,408		61,768
Head and neck					
Cases	230		281		93
Age-adjusted HR (95% CI)	1.00		1.29 (1.09–1.54)		1.33 (1.05–1.69)
Multivariate-adjusted HR ¹ (95% CI)	1.00		1.27 (1.07–1.52)		1.30 (1.02–1.66)
Scalp					
Cases	15		36		33
Age-adjusted HR (95% CI)	1.00		2.56 (1.40–4.68)		7.26 (3.94–13.38)
Multivariate-adjusted HR ¹ (95% CI)	1.00		2.54 (1.39–4.64)		7.09 (3.84–13.08)
Other head and neck sites					
Cases	215		245		60
Age-adjusted HR (95% CI)	1.00		1.21 (1.00–1.45)		0.92 (0.69–1.22)
Multivariate-adjusted HR ¹ (95% CI)	1.00		1.19 (0.99–1.42)		0.90 (0.68–1.20)
Sun-exposed sites other than head and neck					
Cases	95		102		35
Age-adjusted HR (95% CI)	1.00		1.14 (0.86–1.51)		1.25 (0.85–1.85)
Multivariate-adjusted HR ¹ (95% CI)	1.00		1.12 (0.84–1.48)		1.25 (0.84–1.84)
Sun less-exposed sites					
Cases	84		83		25
Age-adjusted HR (95% CI)	1.00		1.05 (0.78–1.43)		1.00 (0.64–1.56)

Squamous cell carcinoma overall Multivariate-adjusted HR / (95% CI)	Male pattern baldness				P for trend
	No	Frontal only	Frontal + mild vertex	Frontal + moderate vertex	Frontal + severe vertex
	1.00		1.03 (0.76–1.39)		0.98
				0.99 (0.63–1.55)	

1 Multivariate-adjusted analyses were performed adjusting for the same variates as listed in the footnote of Table 2.

2 For the analysis by body sites, male pattern baldness was re-classified as three categories: no, moderate (frontal only or with mild vertex baldness), or severe baldness (frontal plus moderate to severe vertex baldness), due to power consideration.