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# Anthropometric features and cutaneous melanoma risk: A prospective cohort study in French women

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#### ABSTRACT

*Background:* Epidemiological studies on anthropometric features and cutaneous melanoma risk in women yielded inconsistent results, with few analyses involving prospective cohort data. Our objective was to explore several anthropometric characteristics in relation to the risk of melanoma in women. *Methods:* We prospectively analysed data from E3N, a French cohort involving 98,995 women born in 1925–1950. Participants completed self-administered questionnaires sent biennially over 1990–2008. Relative risks (RRs) and 95% confidence intervals (CIs) were computed using Cox proportional hazards regression models, adjusted for age, number of naevi, freckling, skin and hair colour, skin sensitivity to sun exposure, residential sun exposure, and physical activity.

*Results:* Height was positively associated with melanoma in age-adjusted models only (RR = 1.27, 95% CI = 1.05–1.55 for  $\geq$ 164 cm vs. <160 cm; *P* for trend = 0.02). After full adjustment, there was a significantly positive relationship between sitting-to-standing height ratio and melanoma risk (RR = 1.40, 95% CI = 1.06–1.86 for  $\geq$ 0.533 vs. <0.518; *P* for trend = 0.02). A large body shape at menarche was inversely associated with the risk of melanoma (RR = 0.78, 95% CI = 0.62–0.98; compared with lean). However, weight, body mass index, body surface area, waist or hip circumference, sitting height or leg length were not significantly associated with risk.

*Conclusion:* These results suggest that height, sitting-to-standing height ratio and body shape at menarche may be associated with melanoma risk. Further research is required to confirm these relationships and better understand the underlying mechanisms.

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# 1. Introduction

Cutaneous melanoma is a potentially lethal cancer for which incidence has risen considerably worldwide over recent decades [1]. Its main risk factors include sun exposure, pigmentary traits

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http://dx.doi.org/10.1016/j.canep.2014.05.008 1877-7821/© 2014 Published by Elsevier Ltd. and familial history of the disease [2]. Associations with other factors are less clear, although evidence suggests a potential influence of sex hormones on melanoma risk [3–5]. Body size has been related to sex hormones [6–8], and some anthropometric characteristics were suggested to be risk factors for cancer in women, particularly breast [9,10], ovary [11], or endometrial [12] cancer. Several epidemiological studies examined the relationships between anthropometric factors and melanoma risk in women, but results have been inconsistent regarding measures of body fatness, and few analyses involved large prospective cohort data. Moreover, most studies generally included a narrow range of characteristics, such as height, weight, body mass index (BMI), and body surface area (BSA). However, other factors, such as components of height or body shapes throughout life, which were suggested to reflect pre-pubertal and pubertal growth [13,14], may

Abbreviations: BMI, body mass index; BSA, body surface area; CI, confidence interval; E3N, Etude Epidémiologique auprès de femmes de l'Education Nationale; IGF, insulin-like growth factor; MET, metabolism equivalent task; RR, relative risk; UVR, ultraviolet radiation; WHR, waist-to-hip ratio.

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also be of interest to better understand the associations between anthropometry and the risk of melanoma. Our objective was to assess the potential relationships between several anthropometric features and the risk of melanoma in women participating in the E3N cohort.

# 2. Methods

## 2.1. The E3N cohort

E3N (Etude Epidémiologique auprès de femmes de l'Education Nationale) is a prospective cohort study involving 98,995 French women born in 1925–1950 and insured by a national health scheme primarily covering teachers. Women were enrolled between 1989 and 1991 after returning a baseline self-administered questionnaire on their lifestyle and medical history along with an informed consent. Follow-up questionnaires were sent every 2–3 years thereafter and addressed medical events such as cancer, which were subsequently confirmed through pathology reports. The E3N cohort received ethical approval from the French National Commission for Computed Data and Individual Freedom (Commission Nationale Informatique et Libertés, CNIL).

## 2.2. Data collection

## 2.2.1. Anthropometric characteristics

Height was collected at baseline and in the 1994, 2000, 2002 and 2005 questionnaires, and self-reported weight was available in each questionnaire. Body mass index (BMI), calculated as weight in kilograms divided by height in metres squared, was computed at each follow-up cycle. We calculated body surface area (BSA) using the formula by Du Bois & Du Bois: BSA ( $m^2$ ) = 0.007184 × weight (kg)<sup>0.425</sup> × height (cm)<sup>0.725</sup> [15]. Self-reported waist and hip circumferences were collected in the 1994, 2002 and 2005 questionnaires. Waist circumference was defined as the smallest circumference between the base of the ribs and the largest point of the iliac crest, while hip circumference was defined as the largest circumference below the umbilicus.

Self-reported sitting height was recorded in 1994, where women were asked to sit upright on a hard seat, buttocks and scapulas against the wall, to measure their height using a tape measure with an angle bracket placed on their heads, and then to subtract the seat height. This allowed to derive a sitting-tostanding height ratio and calculate leg length (as standing height minus sitting height). All anthropometric factors were analysed in tertiles. Body shapes were estimated at inclusion using the figure drawings proposed by Sörensen et al. [16]: women were asked to report the drawing that best reflected their body shape at different ages, with drawings ranking from 1 to 8 corresponding to increasing body size, from the leanest to the largest. The baseline questionnaire recorded body shape at age 8 years, at menarche, at ages 20-25 years, 35-40 years, and at current age. For each of these variables, we created three categories (lean, medium, and large) using a different classification according to the period of life (Table 1).

A validation study of most of these measures was undertaken in 2002 and involved 152 women from the Paris centre of the cohort, who had been clinically examined while providing a blood sample [17]. Correlation coefficients between self-reported and technician-measured anthropometric factors were 0.89 for height, 0.56 for sitting height, 0.94 for weight, 0.92 for BMI, and 0.85 for body shape.

## 2.2.2. Non-anthropometric factors

Pigmentary characteristics were collected at baseline and include hair colour (red, blond, chestnut, brown, or black), skin

#### Table 1

Classification of bod	y shapes at different	ages throughout life	e. E3N cohort.

Lean	Medium	Large
1	2	≥3
≤2	3	$\geq 4$
$\leq 2$	3	$\geq 4$
≤2	3	$\geq 4$
$\leq 2$	3	$\geq 4$
≤3	4	≥5
	$1$ $\leq 2$ $\leq 2$ $\leq 2$ $\leq 2$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$

Body shape drawings as first proposed by Sörensen et al. [16].

<sup>a</sup> Since changes in body shape often occur after menopause, the definition of body shapes was increased by unity in postmenopausal women.

complexion (very fair, fair, medium, dark, or very dark), number of naevi and of freckles (none, few, many, or very many), and skin sensitivity to sun exposure (none, moderate, high). Education was collected at baseline, profession of the father was collected in 1992, and age at menarche was available in the 1990 and 1992 questionnaires. Smoking status was available at each questionnaire but was considered at baseline for the description of the study population. Alcohol consumption and total energy intake were derived from the dietary history questionnaire sent to participants in 1993. Counties of birth and of residence were collected at baseline. Childhood and adult residential sun exposure were estimated by linking these data with a database containing mean daily ultraviolet radiation (UVR) in French counties [18]. Physical activity was assessed in Metabolic Equivalent of Task per hour (MET/h) and was recorded at inclusion and in the 1993, 1997 and 2002 questionnaires, where women were asked to report their time spent walking, biking, swimming, playing tennis, or fitness exercising in a typical week over the past year. To check if socioeconomic status had an impact on our findings, as described in detail elsewhere [19], we computed an index for the income of the participants' father determined by data from income according to professional categories provided by the French National Institute for Statistics and Economic Studies and by using the median category "employee (public service)" as the reference (value of 100) [20].

#### 2.3. Population for analysis

Participants who reported a history of cancer other than basalcell carcinoma at baseline (n = 4788), those who were lost to follow-up from baseline (n = 2207), or who reported to have never menstruated (n = 28) were excluded. Woman-years were computed from the date the first questionnaire was returned to the date of diagnosis of melanoma, date of diagnosis of any other cancer, date of last questionnaire returned, or date of end of follow-up (July 2008), whichever occurred first. For anthropometric variables available from inclusion (and thus involving maximal length of follow-up), the final sample included 91,972 women. For factors available from the 1994 questionnaire only (components of height, waist and hip circumferences), follow-up started on the date the 1994 questionnaire was returned and involved 63,763 women.

#### 2.4. Statistical analysis

Statistical analyses were performed using the SAS statistical software package (version 9.2). We estimated relative risks (RRs) and 95% confidence intervals (CIs) using Cox proportional hazards regression models with age as the time scale. The association between anthropometric factors and melanoma risk was assessed in age-adjusted models, and we then additionally adjusted for pigmentary characteristics, residential sun exposure in childhood

Table 2
Characteristics of study participants, E3N cohort 1990–2008 (n=92,050).

	Incident melanoma				
	Ye	es	No		
	n (589)	% (100)	n (91,461)	% (100)	
Education level					
$\leq 12$ years	60	10.2	12,163	13.3	
13–14 years ≥15 years	323 206	54.8 35.0	47,686 31,612	52.1 34.6	
Father's income index	200	55.0	51,012	54.0	
<93	88	14.9	13,768	15.1	
93-99	91	15.5	13,310	14.5	
100–148 >149	149 136	25.3 23.1	21,484 17,900	23.5 19.6	
≥149 Missing	125	23.1	24,999	27.3	
Hair colour	120	2112	2 1,000	2713	
Blond	97	16.5	9144	10.0	
Red	25	4.2	1518	1.7	
Chestnut Brown	363 84	61.6 14.3	55,175 21,150	60.3 23.1	
Dark	20	3.4	4474	4.9	
Skin complexion					
Very fair	17	2.9	1073	1.2	
Fair	413	70.1	53,239	58.2	
Medium Dark/Very dark	155 4	26.3 0.7	35,680 1469	39.0 1.6	
Number of naevi	-	0.7	1405	1.0	
Very many	143	24.3	9579	10.5	
Many	278	47.2	39,720	43.4	
Few	143	24.3	33,122	36.2	
None Number of freckles	25	4.2	9040	9.9	
Very many	54	9.2	4655	5.1	
Many	222	37.7	26,303	28.8	
Few	138	23.4	22,007	24.0	
None	175	29.7	38,496	42.1	
Skin sensitivity to sun e High	218	37.0	25,771	28.2	
Moderate	283	48.1	44,710	48.9	
None	88	14.9	20,980	22.9	
Smoking status at basel		45.0	12.210	110	
Current smoker Former smoker	84 186	15.0 32.4	13,218 28,135	14.6 31.1	
Non smoker	316	52.4	49,042	54.3	
Alcohol consumption (g					
Non-consumers	70	11.9	8805	9.6	
<8.8 ≥8.8	217	36.8	30,923 30,890	33.8	
≥0.0 Missing	203 99	34.5 16.8	20,843	33.8 22.8	
Physical activity (MET/h		1010	20,010	2210	
<13.8	116	19.7	21,559	23.6	
13.8-19.0	107	18.2	17,660	19.3	
19.1–30.2 ≥30.3	175 191	29.7 32.4	26,331 25,911	28.8 28.3	
Total energy intake (kca		52.4	25,511	20.5	
<1805.53	126	21.4	17,651	19.3	
1805.53-2157.28	137	23.3	17,640	19.3	
2157.29-2561.73	116	19.7	17,661	19.3	
≥2561.74 Missing	111 99	18.8 16.8	17,666 20,843	19.3 22.8	
UVR dose in county of b	-	1010	20,010	2210	
<2.36	142	24.1	19,722	21.6	
2.36-2.47	154	26.2	21,893	23.9	
2.48-2.68 >2.69	132 128	22.4 21.7	20,019	21.9 24.3	
≥2.09 Missing	33	5.6	22,220 7607	8.3	
UVR dose in county of r					
<2.36	141	23.9	19,740	21.6	
2.36-2.47	168	28.5	25,269	27.6	
2.48–2.69 ≥2.70	143 137	24.3 23.3	23,394 23,058	25.6 25.2	
Age at menarche	1.57	و.ري	23,030	23.2	
<13 years	271	46.0	41,499	45.4	
13-14 years	277	47.0	41,204	45.0	
≥15 years Menopausal status <sup>b</sup>	41	7.0	8758	9.6	
Premenopausal	109	18.5	6059	6.6	

Table 2 (Continued)

	Incident melanoma				
	Yes		No		
	n (589)	% (100)	n (91,461) % (10		
Postmenopausal	480	81.5	85,402	93.4	

MET: metabolic equivalent; UVR: ultraviolet radiation.

<sup>a</sup> The cut-off point represents the median level of alcohol consumption in our study population.

<sup>b</sup> At the end of follow-up.

and at baseline, and physical activity. Weight, BMI, BSA, waist and hip circumferences and waist-to-hip circumference ratio (WHR) were considered as time-dependent variables; however, we checked the stability of the results using baseline characteristics only. Tests for linear trend were performed using an ordinal score for each anthropometric factor. We stratified our results according to anatomical site and histological subtype of melanoma using competing-risks models [21]. Tests for homogeneity were performed to compare estimates over strata. Missing data were excluded for each anthropometric factor separately, and figures are provided as footnotes in the tables. For adjustment variables, missing values were imputed to the modal category if occurring in <5% of observations, which has proven to be satisfactory in our data since in this case the risk of bias is low [22]; otherwise a missing category was created.

## 3. Results

During follow-up, 589 melanoma cases (75.5% invasive tumours, 19.5% in situ, 5% unknown) were ascertained in the 92,050 included women. Pathology reports could be obtained for 95% of melanomas and an additional 4.3% of tumours were confirmed by the participants' physicians. Table 2 presents the characteristics of the participants.

#### 3.1. Main analyses

In age-adjusted models, there was a significantly positive relationship between total height and melanoma risk (160-163 cm: RR = 1.20, 95% CI = 0.98−1.48; ≥164 cm: RR = 1.27, 95% CI = 1.05–1.55; compared with <160 cm;  $P_{trend}$  = 0.02), but associations were reduced and no longer statistically significant after full adjustment ( $P_{trend} = 0.12$ ) (Table 3). The factors that attenuated the association between height and melanoma risk were number of naevi and hair colour. However, no major confounding effect could be identified, with a 2-4% change in the RR when hair colour or number of naevi were respectively added in the model. In multivariable models, sitting-to-standing height ratio was positively associated with melanoma risk (0.518-0.532: RR = 1.23, 95% CI = 0.92-1.64; >0.533: RR = 1.40, 95% CI = 1.06–1.86; compared with <0.518;  $P_{trend}$  = 0.02), while there was no significant association with sitting height or leg length.

Weight, BMI, BSA, waist or hip circumference and WHR showed no significant association with melanoma risk. An inverse association was observed between a large body shape at menarche and melanoma risk (RR = 0.78, 95% CI = 0.62–0.98 compared with lean;  $P_{trend}$  = 0.11), while body shapes at other ages were not associated with risk.

#### 3.2. Sensitivity analyses

Results were unchanged when associations between melanoma risk and height or its components were additionally adjusted for educational level, father's income index, age at menarche or BMI.

# Table 3

Relative risks (RRs) and 95% confidence intervals (Cls) for cutaneous melanoma in relation to anthropometric factors, E3N cohort 1990–2008 (n=92,050).

Anthropometric factor <sup>a</sup>	п	Cases	PY	Age-adjusted RR	95% CI	Adjusted RR <sup>b</sup>	95% CI
Height (cm)							
<160	30,101	169	466,104	1.00	-	1.00	-
160–163	27,688	183	427,785	1.20	0.98, 1.48	1.15	0.93, 1.42
≥164	34,197	236	528,275	1.27	1.05, 1.55	1.18	0.97, 1.44
Weight (kg)					$P_{trend} = 0.02$		$P_{trend} = 0.12$
<56	35,220	228	445,119	1.00	_	1.00	-
56-62	28,411	188	435,898	1.04	0.84, 1.28	1.01	0.82, 1.25
≥63	26,355	164	535,140	1.01	0.83, 1.23	0.96	0.78, 1.17
					$P_{trend} = 0.96$		$P_{trend} = 0.63$
BMI (kg/m <sup>2</sup> ) <21.4	36,603	244	475,490	1.00		1.00	
<21.4 21.4–23.8	30,870	201	445,660	0.86	- 0.70, 1.05	0.86	- 0.70, 1.05
≥23.9	22,497	135	494,841	0.86	0.71, 1.05	0.85	0.70, 1.03
223.5	22,457	155	434,841	0.80	$P_{trend} = 0.15$	0.05	$P_{trend} = 0.13$
BSA (m <sup>2</sup> )							
<1.57	33,182	208	438,745	1.00	-	1.00	-
1.57–1.67	30,985	207	474,714	1.07	0.87, 1.32	1.03	0.84, 1.27
≥1.68	25,803	165	502,532	1.12	0.92, 1.38	1.05	0.85, 1.28
Maint singur foren as (am.)C					$P_{trend} = 0.26$		$P_{trend} = 0.67$
Waist circumference (cm) <sup>c</sup> <73	24,176	142	239,104	1.00	_	1.00	_
<73 73–80	24,176	142	253,512	0.93	- 0.72, 1.20	0.92	- 0.71, 1.19
≥81	21,882 15,445	84	253,512	1.06	0.72, 1.20	1.04	0.80, 1.35
<u>~</u> 01	13,773		222,040	1.00	$P_{tren} = 0.66$	1.0-1	$P_{trend} = 0.77$
Hip circumference (cm) <sup>c</sup>					uch		ticna
<94	22,114	128	237,850	1.00	-	1.00	-
94–99	18,333	106	212,957	0.99	0.76, 1.29	0.98	0.75, 1.28
$\geq 100$	20,991	116	263,857	0.96	0.75, 1.24	0.95	0.73, 1.22
					$P_{trend} = 0.77$		$P_{trend} = 0.66$
WHR <sup>c</sup>	24.004	150	242.072	1.00		1.00	
< 0.77	24,894	150	243,073	1.00	-	1.00	-
0.77-0.81	21,046	117	244,035	0.88	0.67, 1.15	0.87	0.67, 1.14
$\geq$ 0.82	15,363	82	226,311	1.16	0.89, 1.49 P <sub>trend</sub> =0.26	1.15	0.88, 1.48 P <sub>trend</sub> = 0.28
Sitting height (cm) <sup>c</sup>					Titena 0120		i trena "oizo
<83	13,290	68	263,693	1.00	-	1.00	-
83-85	15,779	90	186,073	1.14	0.83, 1.56	1.12	0.81, 1.53
$\geq 86$	22,199	143	155,297	1.32	0.99, 1.77	1.26	0.94, 1.68
					$P_{trend} = 0.06$		$P_{trend} = 0.12$
Sitting-to-standing height rat		0.4	100 740	1.00		1.00	
<0.518	16,974	84	198,746	1.00	-	1.00	-
0.518-0.532 ≥0.533	16,803 17,491	101 116	198,364 207,954	1.24 1.37	0.92,1.65 1.03,1.82	1.23 1.40	0.92,1.64 1.06,1.86
≥0.000	17,491	110	207,934	1.57	$P_{trend} = 0.03$	1.40	$P_{trend} = 0.02$
Leg length (cm) <sup>€</sup>					r trena 6165		Tirena 0102
<75	15,994	94	189,615	1.00	-	1.00	-
75–78	17,359	117	204,911	1.16	0.88, 1.52	1.11	0.84, 1.45
$\geq$ 79	17,915	90	210,536	0.86	0.64, 1.15	0.81	0.61, 1.08
					$P_{trend} = 0.30$		$P_{trend} = 0.14$
Body shape at age 8 years Lean	47,071	300	725,313	1.00	_	1.00	_
Medium	47,071 18,106	300 127	281,257	1.00	- 0.90, 1.36	1.00	- 0.89, 1.34
Large	21,280	127	330,400	0.96	0.90, 1.36	0.95	0.89, 1.34
Luige	21,200	150	550,400	0.50	$P_{trend} = 0.86$	0.00	$P_{trend} = 0.79$
Body shape at menarche							incha en o
Lean	47,913	317	738,617	1.00	-	1.00	-
Medium	21,111	156	326,620	1.13	0.93, 1.36	1.12	0.93, 1.36
Large	18,838	98	293,599	0.79	0.63, 0.99	0.78	0.62, 0.98
Pody changest ages 20, 25	276				$P_{trend} = 0.13$		$P_{trend} = 0.11$
Body shape at ages 20–25 ye Lean	ears 46,251	316	714,447	1.00	_	1.00	_
Medium	46,251 29,993	189	464,820	0.92	- 0.77, 1.11	0.92	- 0.77, 1.10
Large	12,662	69	195,412	0.92	0.62, 1.04	0.92	0.62, 1.04
- inge	12,002	05	155,712	0.00	$P_{trend} = 0.08$	0.00	$P_{trend} = 0.08$
Body shape at ages 35–40 ye	ears						
Lean	28,290	202	439,706	1.00	-	1.00	-
Medium	37,508	237	582,201	0.89	0.74, 1.08	0.88	0.73, 1.06
Large	22,974	137	350,849	0.85	0.69, 1.06	0.85	0.68, 1.06
					$P_{trend} = 0.14$		$P_{trend} = 0.12$
Body shape at baseline	20 122	201	460.007	1.00		1.00	
Lean	30,133	201	468,827	1.00	-	1.00	-
Medium	32,594	214	506,506	1.03	0.84, 1.24	1.01	0.83, 1.22

## Table 3 (Continued)

Tuble & (continueu)							
Anthropometric factor <sup>a</sup>	n	Cases	РҮ	Age-adjusted RR	95% CI	Adjusted RR <sup>b</sup>	95% CI
Large	25,585	159	389,026	0.99	0.81, 1.23 $P_{trend} = 0.97$	0.97	0.78, 1.20 $P_{trend} = 0.78$

BMI: body mass index; BSA: body surface area; PY: person-years; WHR: waist-to-hip circumference ratio.

<sup>a</sup> Totals do not add up because missing values were deleted for each anthropometric factor separately: there were 64 (0.07%) missing values for height; 2064 (2.2%) for weight; 2080 (2.3%) for BMI and BSA; 2257 (3.5%) for waist circumference; 2322 (3.6%) for hip circumference; 2457 (3.9%) for WHR; 12,492 (19.6%) for sitting height, sitting-to-standing height ratio, and leg length; 5593 (6.1%) for body shape at age 8 years; 4188 (4.5%) for body shape at menarche; 3144 (3.4%) for body shape at ages 20–25 years; 3328 (3.6%) for body shape at ages 35–40 years; and 3738 (4.1%) for body shape as reported at inclusion

<sup>b</sup> Adjusted for age, hair colour, skin complexion, number of naevi, number of freckles, skin sensitivity to sun exposure, physical activity, and mean ultraviolet radiation dose in counties of birth and of residence at baseline.

<sup>c</sup> Since these factors were available from the 1994 questionnaire, the baseline for these variables is the date the 1994 questionnaire was returned.

No substantial modification was observed when anthropometric factors were mutually adjusted (where relevant). When restricting the analyses to invasive tumours, results were not substantially modified, except for body shape at menarche, for which statistical significance was lost (data not shown). Stratification of analyses according to melanoma site and subtype generally yielded no significant heterogeneity (data not shown), except for body shapes at ages 35–40 years and at baseline between "unknown/rare" melanomas and other subtypes, although difficult to interpret given the diversity of this subgroup.

## 4. Discussion

This prospective study reports significant relationships between sitting-to-standing height ratio, body shape at menarche and melanoma risk.

Among epidemiologic studies exploring anthropometry in relation to melanoma risk in women, we found no previous report on components of height. An association between total height and melanoma has been reported in several studies [23-32], which our findings confirm in age-adjusted models, although the results were no longer statistically significant after full adjustment. Proposed explanations for the associations between height or its components and melanoma risk have included the direct association between height and number of susceptible melanocytes [27]. However, our data do not confirm this hypothesis since we found no significant association between BSA and melanoma risk, consistent with the finding from a recent meta-analysis on obesity in relation to melanoma risk [33]. Menarcheal age could represent a confounding factor of the relation between height or its components and melanoma risk, since menarcheal age influences total height [34] and that later menarche was associated with reduced melanoma risk in our cohort [5]; however, our results were identical after adjustment for this factor.

This is the first study to report associations between some components of heights, i.e. sitting-to-standing height ratio, and melanoma risk. A limitation of this result pertains to the lower correlation between self-reported and measured sitting height than for the other studied anthropometric parameters in the validation study [17], which may indicate that this feature is difficult to reliably measure. However, observed associations were quite strong, and overestimation of effects due to systematic measurement errors is improbable, since measurement errors of sitting height are unlikely to be differential between cases and non-cases. Thus, the expected effect of the probable misclassification across tertiles would be a reduction of the true association, but also a reduction of any existing dose-effect relationship. Alternatively, there may be a threshold effect, with a reduced melanoma risk for small sitting height. While sitting height and leg length were not significantly associated with melanoma risk, we observed a significant association between sitting-to-standing height ratio, which may indicate that the effect of height components is not absolute but rather relative to total height. If confirmed, our results could indicate an influence of childhood or pubertal insulin-like growth factor I (IGF-I) levels in melanoma development, since IGF-I has shown proliferative effects on melanoma cells in vitro [35] and a higher sitting height may reflect a stronger pubertal growth spurt [36], and thus greater growth hormone and IGF-I surges during peak growth [14]. More research is needed to understand these complex processes. Alternatively, socio-economic status may be a confounder of the association between height, its components and melanoma risk. However, our findings were not substantially modified after adjustment for education level or father's income index, although it should be noted that this cohort is quite homogeneous in terms of education and socio-economic status.

Our findings of a null association between weight and melanoma risk are consistent with those from most studies [27,28,37–39]. Regarding BMI, the meta-analysis reported no significant association with melanoma risk in females [33]. However, among analyses adjusting for sun exposure, casecontrol studies yielded a significantly positive association between obesity and melanoma risk, while cohort studies yielded a significantly inverse association. Our result of an inverse association between BMI and melanoma risk, albeit not statistically significant, is consistent with the latter report, although it contrasts with a recent prospective cohort study that showed inverse associations between BMI and the risk of non-melanoma skin cancers, but not melanoma [40]. We found no previous report on melanoma risk in relation to waist or hip circumferences, or body shapes at different ages. Larger body size in childhood has been associated with hyperinsulinaemia [41] and anovulatory cycles [42], as well as increased levels of estrogens and other sex hormones [43,44]. Since melanoma risk may be associated with hormonal factors, our observed inverse association with body shape at menarche could suggest a reduced risk with early exposure to sex hormones, similar to what has been proposed for breast cancer [9]. However, although results were stable after adjustment for residential sun exposure in our study, we were unable to adjust for behavioural sun exposure, and variability in sun exposure patterns (e.g. lower exposure in overweight women) may confound the relationship between melanoma and body fat characteristics.

Strengths of our study include the large sample size and prospective design with repeated updates of anthropometric features over a long follow-up period. This is the first study investigating components of heights and body shapes in relation to melanoma risk in women. Self-reported anthropometric factors were validated and generally showed high repeatability levels, except for sitting height, for which reproducibility was only moderate [17], as described above. However, although our cohort sample size is large, we may have lacked power to observe a significant association between height, its components and melanoma risk. While most previous studies on total height in relation to melanoma risk were case-control studies including smaller sample sizes than that available in our cohort [27], other cohort studies [25,29,32], although not all [26,30,31,38,45], had a larger statistical power to observe significant associations with height. Another limitation is our lack of behavioural sun exposure data, although reliable data on residential sun exposure were adjusted for. This may have hampered our ability to control for behavioural factors towards the sun that may be associated with body fatness measures.

In conclusion, this is the first report of an association between sitting-to-standing height ratio, body shapes and melanoma risk in women. More research is warranted to confirm these relationships and better understand their underlying mechanisms.

#### **Conflict of interest**

The authors have no conflict of interest to disclose.

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