Br J Dermatol 2023; **00**:1–3
https://doi.org/10.1093/bjd/ljac136
Advance access publication date: 21 December 2022

BJD
British Journal of Dermatology
Research Letter

No association between physical activity and primary melanoma thickness in a cohort of Norwegian women

Dear Editor, Knowledge about factors associated with melanoma thickness, the most important prognostic factor for localized primary melanoma survival,[1] may help reduce the risk of melanoma deaths. Previously reported associations of melanoma thickness with pigmentary characteristics, number of naevi, diet quality and body mass index (BMI)[2–4] may be explained by behavioural and biological mechanisms. Physical activity (PA) has been associated with improved outcomes for several cancers,[5] but its relation with melanoma thickness and prognosis is unknown.

We investigated the association between PA and melanoma thickness at diagnosis, a surrogate for risk of death, in the large population-based Norwegian Women and Cancer (NOWAC) cohort. All women provided informed consent, and data were handled in accordance with the relevant ethical regulations. The study was approved by the Regional Committees for Medical and Health Research Ethics of North Norway (2021/252094/REK Nord) and the Norwegian Centre for Research Data (2021/147992). The data generated and/or analysed in the current study can be accessed upon reasonable request to the originating cohort. Access will be conditional on adherence to local ethical and security policy. The R code used to conduct specific analyses will be shared on reasonable request (of the specific code) to the corresponding author.

Questionnaires were sent in 1991–2007 to over 320 000 women aged 30–75 years, randomly drawn from the Norwegian National Population Register. Participants reported their current level of PA referring to overall PA across different domains (recreational, occupational, transport, housework) using a validated 10-point scale,[6] categorized as low (1–4), moderate (5–6) and high (7–10). They also reported pigmentary characteristics (hair, eye and skin colour, number of asymmetric naevi > 5 mm on the legs, freckling), BMI, education and ultraviolet radiation (UVR) exposure (ambient UVR of residence, annual number of severe sunburns). A pigmentary score summarizing information on hair, eye and skin colour and freckling was created, and categorized as dark, medium and fair.[2]

Using the unique 11-digit identity number of Norwegian citizens, the NOWAC cohort was linked to the Cancer Registry of Norway and the Norwegian National Population Register for information on cancer incidence, emigration and death. Among the 172 000 participants, first incident primary invasive melanoma was diagnosed for 2437 women. After exclusion of women who did not receive ($n = 5$) or answer the PA question ($n = 87$), had prevalent cancer ($n = 780$) or had missing information on melanoma thickness ($n = 121$), 1444 melanoma cases were included in the analyses. Melanoma thickness (mm) at diagnosis was categorized as T1 (≤ 1.0), T2 (> 1.0–2.0), T3 (> 2.0–4.0) and T4 (> 4.0).[1] Based on the International Classification of Diseases 7th Revision, anatomical site was categorized as head/neck (190.0), trunk (190.1/190.7), upper limb (190.2), lower limb (190.3/190.4), multiple sites (190.8) and unspecified site (190.9), and melanoma subtypes as superficial spreading melanoma (87433), nodular melanoma (87213) and other (lentigo maligna 87423, acral lentiginous 87443, other 87453/87803/87613 and unspecified 87203).

Under the assumption of missing at random, multiple imputation by chained equations was used to impute missing values in BMI, pigmentary score, education, naevi and sunburns. The association between PA and melanoma thickness was assessed by ordinal logistic regression, and the probability of being diagnosed with each T-category was calculated for low, medium and high PA categories, respectively. We adjusted for age at baseline and at melanoma diagnosis, BMI, pigmentary score, education, number of asymmetric naevi, number of sunburns and ambient UVR of residence, and stratified by anatomical site and melanoma subtype.

Among the 1444 melanoma cases, 906 (63%) were T1, 312 (22%) T2, 160 (11%) T3 and 66 (5%) T4. No association between PA and melanoma thickness was found for melanoma overall (Figure 1): across all PA levels, the probabilities of being diagnosed with a T1 melanoma were 57–62%, T2 22–24%, T3 11–13% and T4 5–6%. Similar results were found for lower limb melanoma. Compared with low activity, slightly thinner upper limb melanomas (T1) were predicted for highly active cases, while thicker melanomas (T2, T3 or T4) were predicted on the trunk, but these associations were not significant. No associations were found when stratifying by melanoma subtype (results not shown).

The strengths of this study include population-based data in a prospective cohort study representative of Norwegian women aged 30–75 years,[7] with follow-up through national registers, PA recorded before melanoma diagnosis, and a self-reported PA scale found valid to rank PA level in Norwegian women.[6] We lacked information on outdoor/indoor PA and on behaviours like skin checks that favour melanoma early detection with low thickness, but we adjusted for education, which was sufficient to estimate the total effect of PA on thickness according to our directed acyclic graph. To our knowledge, only one study has reported on PA and melanoma survival[8] and only one on PA and melanoma thickness;[3] both found no association, in line with our results in Norwegian women. We conclude that PA is unlikely to be associated with melanoma thickness.

Accepted: 13 December 2022

Anatomical site	Thickness	Low PA	Moderate PA	High PA
Whole body,	T1	0.57 (0.38–0.74)	0.62 (0.42–0.78)	0.57 (0.37–0.75)
n = 1444	T2	0.24 (0.13–0.41)	0.22 (0.11–0.39)	0.24 (0.12–0.42)
	T3	0.13 (0.07–0.25)	0.11 (0.05–0.22)	0.13 (0.06–0.26)
	T4	0.06 (0.03–0.11)	0.05 (0.02–0.10)	0.06 (0.03–0.12)
Trunk,	T1	0.78 (0.46–0.94)	0.73 (0.38–0.93)	0.68 (0.32–0.91)
n = 487	T2	0.14 (0.04–0.40)	0.16 (0.04–0.46)	0.19 (0.05–0.51)
	T3	0.06 (0.02–0.21)	0.08 (0.02–0.27)	0.09 (0.02–0.32)
	T4	0.02 (0.01–0.09)	0.03 (0.01–0.12)	0.04 (0.01–0.15)
Upper limb,	T1	0.44 (0.19–0.73)	0.56 (0.25–0.82)	0.50 (0.21–0.80)
n = 254	T2	0.30 (0.11–0.60)	0.26 (0.09–0.57)	0.28 (0.09–0.60)
	T3	0.17 (0.06–0.42)	0.12 (0.04–0.34)	0.14 (0.04–0.40)
	T4	0.09 (0.03–0.25)	0.06 (0.02–0.18)	0.07 (0.02–0.23)
Lower limb,	T1	0.67 (0.24–0.93)	0.77 (0.32–0.96)	0.81 (0.38–0.97)
n = 558	T2	0.22 (0.04–0.65)	0.16 (0.03–0.57)	0.13 (0.02–0.52)
	T3	0.09 (0.02–0.40)	0.06 (0.01–0.30)	0.05 (0.01–0.26)
	T4	0.02 (0.00–0.13)	0.01 (0.00–0.09)	0.01 (0.00–0.07)

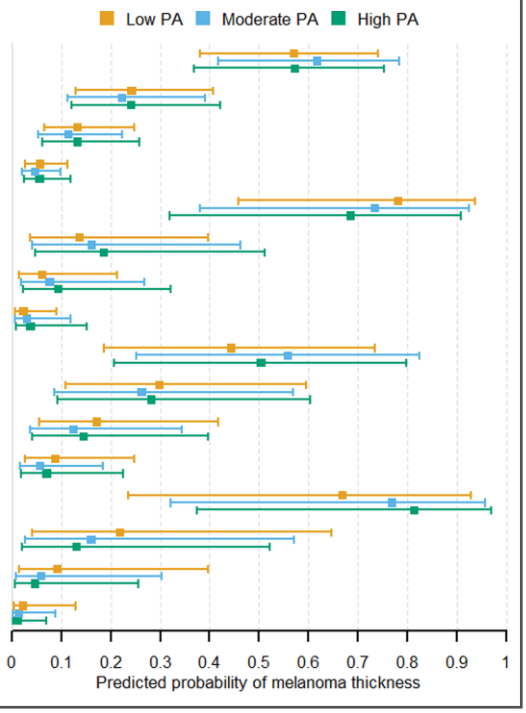

Figure 1 Predicted probabilities and 95% confidence intervals of melanoma thickness categories according to physical activity (PA) level, for first primary invasive melanomas (*n* = 1444), stratified by anatomical site, in the Norwegian Women and Cancer cohort, 1991–2018. Missing values in body mass index (BMI) (2.0%), education (4.6%), pigmentary score (25.0%), sunburn (11.2%) and number of asymmetric naevi (12.0%) were imputed with multiple imputations by chained equations using additional information on ages at baseline and diagnosis, region of residence, birth cohort, year of questionnaire completion, smoking, indoor tanning, and sunbathing vacations. BMI was obtained from imputed height (0.8% missing) and weight (1.8% missing), and pigmentary score from imputed hair, eye, skin and freckling scores (6.5%, 6.7%, 18.0% and 16.0% missing, respectively). Fifty imputed datasets were created using 50 iterations. Ordinal logistic regression adjusted for age at baseline and at melanoma diagnosis, BMI, pigmentary score, education, number of asymmetric naevi, number of sunburns and ambient UVR of residence was performed in each imputed dataset, and results were pooled using Rubin's rules. Results for head and neck are not presented, as the number of melanoma cases per cell of the cross-table between PA and thickness was too low (*n* = 119, range 0–32 per cell). T-categories = melanoma thickness (mm), defined as: T1: ≤1.0; T2: >1.0–2.0; T3: >2.0–4.0; T4: >4.0.

Flavie Perrier[1], **Trude E. Robsahm**[2], **Reza Ghiasvand**[2,3], **Kristin B. Borch**[4], **Tonje Braaten**[4], **Elisabete Weiderpass**[5], **Corina S. Rueegg**[3], **Adele C. Green**[6,7] **and Marit B. Veierød**[1]

[1]Oslo Centre for Biostatistics and Epidemiology, Department of Biostatistics, Institute of Basic Medical Sciences, University of Oslo, Oslo, Norway; [2]Cancer Registry of Norway, Institute of Population-Based Cancer Research, Oslo, Norway; [3]Oslo Centre for Biostatistics and Epidemiology, Oslo University Hospital, Oslo, Norway; [4]Department of Community Medicine, Faculty of Health Sciences, UiT The Arctic University of Norway, Tromsø, Norway; [5]International Agency for Research on Cancer, Lyon, France; [6]QIMR Berghofer Medical Research Institute, Brisbane, QLD, Australia; [7]Cancer Research UK Manchester Institute and Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK

Correspondence: Flavie Perrier. Email: flavie.perrier@medisin.uio.no

Acknowledgments: the authors are grateful to all the women who participated in the NOWAC cohort and without whom this work would not have been possible.

Funding sources: this work was supported by the Norwegian Cancer Society (project 197975 to F.P.). The funding source had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; and decision to submit the manuscript for publication.

Conflicts of interest: the authors declare they have no conflicts of interest.

References

1 Gershenwald JE, Scolyer RA, Hess KR *et al.* Melanoma staging: evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. *CA Cancer J Clin* 2017; **67**:472–92.
2 Ghiasvand R, Green AC, Sandanger TM *et al.* Phenotypic characteristics and melanoma thickness in women. *Acta Derm Venereol* 2021; **101**:adv00446.
3 Hardie CM, Elliott F, Chan M *et al.* Environmental exposures such as smoking and low vitamin D are predictive of poor outcome in cutaneous melanoma rather than other deprivation measures. *J Invest Dermatol* 2020; **140**:327–37.e2.
4 Hughes MCB, Malt M, Khosrotehrani K *et al.* Diet quality is associated with primary melanoma thickness. *J Eur Acad Dermatol Venereol* 2022; **36**:1745–50.
5 Ballard-Barbash R, Friedenreich CM, Courneya KS *et al.* Physical activity, biomarkers, and disease outcomes in cancer survivors: a systematic review. *J Natl Cancer Inst* 2012; **104**:815–40.
6 Borch KB, Ekelund U, Brage S, Lund E. Criterion validity of a 10-category scale for ranking physical activity in Norwegian women. *Int J Behav Nutr Phys Act* 2012; **9**:2.

7 Lund E, Kumle M, Braaten T *et al.* External validity in a population-based national prospective study – the Norwegian Women and Cancer Study (NOWAC). *Cancer Causes Control* 2003; **14**:1001–8.

8 Schwitzer E, Orlow I, Zabor EC *et al.* No association between prediagnosis exercise and survival in patients with high-risk primary melanoma: a population-based study. *Pigment Cell Melanoma Res* 2017; **30**:424–7.