

LETTER TO THE EDITOR

Physical activity is associated with improved survival in skin cancer patients: A meta-analysis

Dear Editor,

Cutaneous melanoma (CM) and non-melanoma skin cancers (NMSC) are highly incident malignancies with a growing health burden. Despite improvements in systemic therapies, the identification of actionable prognostic factors remains crucial to support an integrated approach to patient management. Physical activity is generally associated with improved survival for patients with cancer, but evidence regarding its prognostic role in skin cancer remains limited, providing rationale for this PRISMA-compliant systematic review and meta-analysis.

Literature search was conducted in PubMed and EMBASE on September 3rd, 2025. We targeted studies reporting on the association between pre-/post-diagnosis physical activity and survival in patients with CM or NMSC. Any type of physical activity (e.g. recreational, at work or total) was considered. Random-effects models were used to calculate summary hazard ratio (sHR) and 95% confidence intervals (CI) for overall (OS), cancer-specific (CSS) and non-cancer-specific survival (NCSS). Heterogeneity between studies was quantified using the I^2 statistics, and pre-planned subgroup

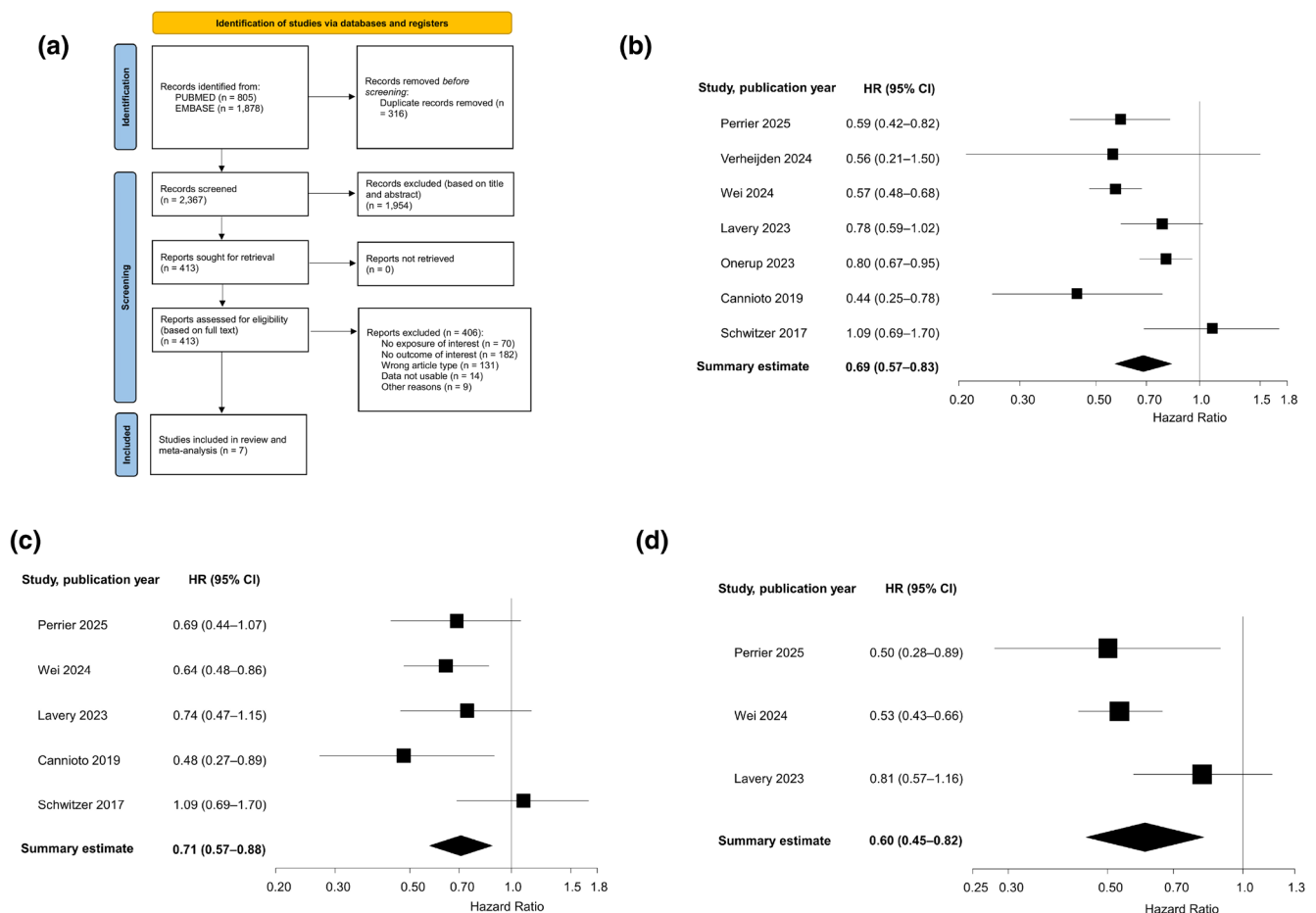


FIGURE 1 Systematic review and meta-analysis for the association between physical activity and survival of patients with skin cancer (cutaneous melanoma and non-melanoma skin cancer): PRISMA flow diagram for the selection of studies (a) and forest plots for overall survival (b), cancer-specific survival (c) and non-cancer-specific survival (d). CI, confidence intervals; HR, hazard ratio.

TABLE 1 Selected characteristics of the studies included in the systematic review and meta-analysis on the association between physical activity and prognosis of patients with skin cancer.

Author, year	Country	No. patients by skin cancer type	Demographics	Follow-up (mean/median)	Physical activity type	Physical activity measurement	Exposure timing	Endpoint(s)	Adjustments
Perrier, 2025 ²	Norway	1829 CM	100% women, mean age 63.2 years	8.3 years	Total	10-point scale	Post-diagnosis	OS, CSS, NCSS	Age, stage, smoking, other
Verheijden, 2024 ³	Netherlands	153 CM + 66 NMSC + 32 skin NOS	66.5% men, mean age 64 years	1 year	Total	SQUASH questionnaire, MET-hours/week	Post-diagnosis	OS	Age, sex, stage, other
Wei, 2024 ⁴	USA	924 skin NOS	47.8% men, median age 65 years	5.7 years	Total	Global Physical Activity Questionnaire (GPAQ), MET-min/week	Post-diagnosis	OS, CSS, NCSS	Age, sex, smoking, alcohol, other
Lavery, 2023 ⁵	USA	773 CM	NA	16 years	Strenuous or moderate exercise	12-items questionnaire, comparison to adherence to national guidelines	Pre-diagnosis	OS, CSS, NCSS	Age, sex, stage, other
Onerup, 2023 ⁶	Sweden	28,418 skin NOS	100% men, mean age 52.5 years	6.5 years	Cardiorespiratory fitness	Ergometer test, score	Pre-diagnosis	OS	Age, other
Cannioto, 2019 ⁷	USA	347 skin (95% CM)	NA	4.9 years	Recreational	DBBR questionnaire, habitually active/inactive	Pre- and post-diagnosis	OS, CSS	Age, sex, stage, smoking
Schwitzer, 2017 ⁸	USA	2465 CM	NA	NA	Recreational	Baseline study questionnaire, MET-hours/week	Post-diagnosis	CSS	Age, sex, smoking, alcohol, other

Abbreviations: CM, cutaneous melanoma; CSS, cancer-specific survival; DBBR, Roswell Park Data Bank and BioRepository questionnaire; MET, metabolic equivalent of task; NA, not available; NCSS, non-cancer-specific survival; NMSC, non-melanoma skin cancer; NOS, not otherwise specified; OS, overall survival; SQUASH, Short Questionnaire to Assess Health Enhancing Physical Activity.

analyses were conducted. Study quality was assessed using the Quality in Prognosis Studies (QUIPS).¹

A total of seven articles^{2–8} published between 2017 and 2025 were included, with the selection process shown in Figure 1a and study characteristics in Table 1. Study quality was generally fair. The sHR for OS was 0.69 (95% CI 0.57–0.83, $I^2 = 61.1\%$) (Figure 1b), highlighting lower all-cause mortality risk among more physically active individuals. In meta-regression, post-diagnosis activity was associated with a survival benefit (sHR 0.57, 95% CI 0.48–0.68, $n = 2$) stronger than pre-diagnosis activity (sHR 0.78, 95% CI 0.69–0.89, $n = 4$), p for difference = 0.004. Similarly, the association with survival was stronger in studies using validated (sHR 0.57, 95% CI 0.49–0.67, $n = 3$) vs. non-validated (sHR 0.74, 95% CI 0.47–1.18, $n = 3$) physical activity questionnaires, p for difference = 0.026. For CSS, based on five studies, the sHR was 0.71 (95% CI 0.57–0.88, $I^2 = 22.4\%$) (Figure 1c). A stronger association was observed for NCSS, based on three studies (sHR 0.60, 95% CI 0.45–0.82, $I^2 = 53.7\%$) (Figure 1d). In a sensitivity analysis, we included only the studies whose population consisted entirely of patients with CM and merged estimates for CSS (four studies) and OS (the single study by Onerup et al. 2023): the

pooled HR was 0.78 (95% CI 0.68–0.90, $I^2 = 0\%$). Excluding the one study which used cardiorespiratory fitness as a surrogate of physical activity, the results were unchanged (sHR 0.66, 95% CI 0.52–0.83). Additional sensitivity and subgroup analyses largely confirmed the observed results across physical activity types and endpoints. No evidence of publication bias was detected.

Several plausible mechanisms may explain the reduced mortality observed among physically active patients with skin cancer, including anti-inflammatory, metabolic and immune-mediated effects. Physical activity exerts anti-inflammatory and metabolic effects, lowering insulin and IGF-1 signalling and reducing chronic inflammatory mediators, which are linked to cancer progression and mortality across tumour types.⁹ In addition, physical activity can significantly mitigate the side effects of cancer therapies and improve prognosis by modulating immune responses and optimizing metabolic pathways, potentially synergizing with immunotherapy, particularly in advanced melanoma.¹⁰ This meta-analysis has some limitations, including the moderate number of studies (mostly relying on self-reported physical activity) and the absence of randomized trials. Residual confounding by disease stage, comorbidities,

treatment and lifestyle-related factors cannot be excluded. Nonetheless, the consistency of the results (across skin cancer subtypes, survival endpoints and type of physical activity), their biological plausibility and the evidence highlighting the relevance of post-diagnosis exercise support the notion that physical activity may represent a safe, feasible and high-impact intervention that should be integrated into survivorship care for patients with skin cancer in addition to standard treatments.

KEYWORDS

melanoma, meta-analysis, physical activity, prognosis, skin neoplasms, survival analysis, systematic review

FUNDING INFORMATION

This study was partially funded by the Italian Ministry of Health Ricerca Corrente with 5×1000 funds.

CONFLICT OF INTEREST STATEMENT

All authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICAL APPROVAL

Not applicable.

ETHICS STATEMENT

Not applicable.

Alessandra Picelli¹
Aurora Gaeta^{2,3}
Chiara Doccioli⁴
Francesco Tanzi²
Maristella Saponara⁵
Daniela Massi^{6,7}
Calogero Saieva⁸
Giulio Tosti⁹
Ines Zanna⁸
Patrizia Gnagnarella¹⁰
Mario Mandalà¹¹ 
Enrica Castellana¹
Ignazio Stanganelli^{12,13}
Saverio Caini⁸ 
Sara Gandini²

¹Medical Specialization School of Hygiene and Preventive Medicine, University of Florence, Florence, Italy

²Department of Experimental Oncology, IRCCS European Institute of Oncology, Milan, Italy

³Department of Statistics and Quantitative Methods, University of Milano-Bicocca, Milan, Italy

⁴Clinical Epidemiology Unit, Institute for Cancer Research, Prevention, and Clinical Network (ISPRO), Florence, Italy

⁵Melanoma Medical Treatment Unit, IRCCS European Institute of Oncology, Milan, Italy

⁶Section of Pathology, Department of Health Sciences, University of Florence, Florence, Italy

⁷Department of Molecular Pathobiology, New York University - College of Dentistry, New York, New York, USA

⁸Cancer Risk Factors and Lifestyle Epidemiology Unit, Institute for Cancer Research, Prevention, and Clinical Network (ISPRO), Florence, Italy

⁹Dermato-Oncology Unit, IEO European Institute of Oncology IRCCS, Milan, Italy

¹⁰Division of Epidemiology and Biostatistics, IEO European Institute of Oncology IRCCS, Milan, Italy

¹¹Unit of Medical Oncology, Department of Medicine and Surgery, University of Perugia, Perugia, Italy

¹²School of Dermatology, Residency Training Program, Department of Medicine and Surgery, University of Parma, Parma, Italy

¹³Skin Cancer Unit, IRCCS Istituto Romagnolo per Lo Studio Dei Tumori 'Dino Amadori' - IRST, Meldola, Italy

Correspondence

Saverio Caini, Cancer Risk Factors and Lifestyle Epidemiology Unit, Institute for Cancer Research, Prevention, and Clinical Network (ISPRO), Via Cosimo il Vecchio 2, 50139 Florence, Italy.
Email: s.caini@ispro.toscana.it

Alessandra Picelli and Aurora Gaeta contributed equally to this study and co-first authors.

ORCID

Mario Mandalà  <https://orcid.org/0000-0001-8846-8959>
Saverio Caini  <https://orcid.org/0000-0002-2262-1102>

REFERENCES

- Hayden JA, van der Windt DA, Cartwright JL, Côté P, Bombardier C. Assessing bias in studies of prognostic factors. *Ann Intern Med.* 2013;158(4):280–6.
- Perrier F, Ahimbisibwe A, Ghiasvand R, Rueegg CS, Green AC, Borch KB, et al. Physical activity and mortality in melanoma patients within the Norwegian Women and Cancer study (NOWAC). *Int J Cancer.* 2025;157(5):846–57.
- Verheijden RJ, Cabané Ballester A, Smit KC, van Eijs MJM, Bruijnen CP, van Lindert ASR, et al. Physical activity and checkpoint inhibition: association with toxicity and survival. *J Natl Cancer Inst.* 2024;116(4):573–9.
- Wei X, Min Y, Xiang Z, Zeng Y, Wang J, Liu L. Joint association of physical activity and dietary quality with survival among US cancer survivors: a population-based cohort study. *Int J Surg.* 2024;110(9):5585–94.
- Lavery JA, Boutros PC, Scott JM, Tammela T, Moskowitz CS, Jones LW. Pan-cancer analysis of postdiagnosis exercise and mortality. *J Clin Oncol.* 2023;41(32):4982–92.
- Onerup A, Mehlig K, Ekblom-Bak E, Lissner L, Börjesson M, Åberg M. Cardiorespiratory fitness and BMI measured in youth and 5-year mortality after site-specific cancer diagnoses in men: a population-based cohort study with register linkage. *Cancer Med.* 2023;12(19):20000–14.

7. Cannioto RA, Dighe S, Mahoney MC, Moysich KB, Sen A, Hulme K, et al. Habitual recreational physical activity is associated with significantly improved survival in cancer patients: evidence from the Roswell Park Data Bank and BioRepository. *Cancer Causes Control*. 2019;30(1):1–12.
8. Schwitzer E, Orlov I, Zabor EC, Begg CB, Berwick M, Thomas NE, 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(4):424–7.
9. Jurdana M. Physical activity and cancer risk. Actual knowledge and possible biological mechanisms. *Radiol Oncol*. 2021;55(1):7–17.
10. Misiąg W, Piszczek A, Szymańska-Chabowska A, Chabowski M. Physical activity and cancer care-a review. *Cancers (Basel)*. 2022;14(17):4154.