Journal of Physical Activity and Health, (Ahead of Print)
https://doi.org/10.1123/jpah.2024-0390

First Published Online: Jan. 21, 2025

Human Kinetics
BRIEF REPORT

Physical Activity and Life Expectancy Free of Cancer: Prospective Evidence From the UK Biobank Study

Miguel Adriano Sanchez-Lastra,[1,2,3] Borja del Pozo Cruz,[4,5] Ulf Ekelund,[3,6] Jakob Tarp,[3] and Ding Ding[7,8]

[1]Department of Special Didactics, Faculty of Education and Sports Sciences, University of Vigo, Pontevedra, Spain; [2]Well-Move Research Group, Galicia-Sur Health Research Institute (SERGAS-UVIGO), Vigo, Spain; [3]Department of Sports Medicine, Norwegian School of Sport Sciences, Oslo, Norway; [4]Faculty of Sport Sciences, Universidad Europea de Madrid, Villaviciosa de Odón, Madrid, Spain; [5]Center for Active and Healthy Aging, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark; [6]Department of Chronic Diseases, Norwegian Institute of Public Health, Oslo, Norway; [7]Prevention Research Collaboration, Sydney School of Public Health, The University of Sydney, Camperdown, NSW, Australia; [8]Charles Perkins Center, The University of Sydney, Camperdown, NSW, Australia

Background: Life expectancy free of cancer (LEFC) is a novel measure that considers both morbidity and mortality and could be a useful metric for disease surveillance and risk communication. We aimed to examine the association between physical activity and LEFC in British adults. ***Methods:*** This was a prospective cohort study of 292,559 apparently healthy UK Biobank participants (mean [SD] age, 56.0 [8.1] y, 51% women). Participants were categorized based on self-reported physical activity as "no activity" (0 min/wk), "insufficiently active" (10–599 metabolic equivalent-min/wk), "active" (600–1199 metabolic equivalent-min/wk), and "very active" (>1200 metabolic equivalent-min/wk). Hazard ratios from multistate models for transitions between 3 states (cancer-free, cancer diagnosis, and all-cause mortality) were used to calculate differences in predicted remaining LEFC across physical activity levels for men and women at ages 45 and 65 years. ***Results:*** During a median follow-up of 11.0 years, we recorded 13,143 cancer cases for men and 10,255 for women, and 6488 deaths for men and 3739 for women. At age 45, "insufficiently active," "active," and "very active" had a higher LEFC by 2.35, 2.46, and 2.76 years compared with "no activity," and by 1.44, 1.62, and 1.84 years at age 65. In women, the "insufficiently active," "active," and "very active" had a higher LEFC by 1.09, 1.42, and 1.59 years at age 45, and by 1.25, 1.54, and 1.71 years at age 65. ***Conclusions:*** Engaging in physical activity, even below recommended levels, appears to extend cancer-free years of life. Promoting physical activity is an important strategy for cancer prevention.

Keywords: morbidity, mortality, chronic disease, public health, health behavior

Key Points

- Physical activity, even below recommended levels, was associated with higher life expectancy free of cancer, with men gaining up to 2.76 years and women up to 1.59 years at age 45, and up to 1.84 and 1.71 years, respectively, at age 65, compared to those who were inactive.
- Promoting physical activity, even at low levels, may be useful for extending cancer-free years and enhancing cancer prevention strategies.

Cancer is a leading cause of death[1] and an economic burden worldwide.[2] It is estimated that 30% to 50% of all cancer cases could be prevented.[3] Physical activity is increasingly regarded as a key component for cancer prevention in the general population[4,5] and it plays a critical role in improving physical functioning, quality of life, and potential survival in cancer patients.[6]

With a lifetime risk of cancer above 50%,[7] epidemiological research should not only consider occurrence of cancer, but also the age of occurrence, and years lived after diagnosis. Multistate models simultaneously take into account various disease states, such as illness, and death and have been increasingly applied to cancer research.[8] Furthermore, interpreting statistics, such as hazard ratios (HRs), can be challenging for the general population. Life expectancy free of cancer (LEFC) is a novel measure that takes into account both morbidity, and mortality, and could be a useful metric for disease surveillance and risk communication. As a novel indicator, LEFC was only applied by a small number of studies recently.[9,10] In this study, we examined the association between physical activity and LEFC in British adults.

Methods

Data are from the UK Biobank, a large population-based cohort study. Between 2006 and 2010, 502,632 participants aged 37–82 were recruited throughout the United Kingdom for baseline assessment. Ethical approval was obtained from the North-West Research Ethics Committee and details about the cohort have been previously published.[11] We followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines (see

del Pozo Cruz https://orcid.org/0000-0003-3944-2212
Ekelund https://orcid.org/0000-0003-2115-9267
Tarp https://orcid.org/0000-0002-9186-7077
Ding https://orcid.org/0000-0001-9850-9224
Sanchez-Lastra (misanchez@uvigo.gal) is corresponding author, https://orcid.org/0000-0001-7457-3475

Supplementary Table S1 in Supplementary Material [available online]).

Physical activity (including work, transport, domestic, and leisure-time activities) was measured at baseline (2006–2010) using the short version of the International Physical Activity Questionnaire, which has established reliability and validity.[12] Following the International Physical Activity Questionnaire protocol,[13] we summed metabolic equivalent (MET) of walking (3.3 METs), moderate-intensity (4 METs), and vigorous-intensity (8 METs) physical activity that lasted for at least 10 minutes, and categorized participants into "no activity" (0 min/wk), "insufficiently active" (10–599 MET-min/wk), "active" (600–1199 MET-min/wk), and "very active" (1200+ MET-min/wk) according to the World Health Organization's Guidelines on Physical Activity and Sedentary Behavior.[14] Total malignant cancer incidence (excluding nonmelanoma skin cancer) was ascertained from registries incorporating diagnoses from diverse sources, including hospitals and treatment centers. The date of death was ascertained from death certificates held by the National Health Service. Participants were censored on February 29, 2020 for England and Wales and January 31, 2021 for Scotland.

We used nonrecoverable multistate models to estimate how participants transitioned between the following states: free of cancer (state 1), cancer diagnosis (state 2), and all-cause mortality (state 3). We used a Markov semiparametric model and a Weibull distribution to estimate the HRs and 95% confidence intervals (CIs) associated with each of the 3 possible transitions: from states 1 to 2 (transition 1), 1 to 3 (transition 2), and 2 to 3 (transition 3). We did not allow for backward transitions from states 2 to 1. After excluding individuals with preexisting poor health, underweight, pregnant, or unable to walk at baseline, and with less than 2 years of follow-up (see Supplementary Figure S1 in Supplementary Material [available online]), we adjusted our models for age; education; ethnicity; postcode-level deprivation; marital status; smoking; alcohol consumption; diet; body fat percentage; screen time; and preexisting depression, diabetes, or hypertension. For women, models were additionally adjusted for age at menarche, parity, oral contraceptive use, menopause, and hormone replacement therapy use. We then used these adjusted transition-specific HRs to predict and compare the expected number of remaining years of life free of cancer by physical activity level, conditional of reaching 100 years of age.[10] We presented the results as differences in predicted remaining LEFC across physical activity levels for men and women at ages 45 and 65 years. We left truncated the first 2 years of follow-up, and modeled men and women separately, and set the alpha at .05. We conducted a sensitivity analysis limiting cancer outcomes to the types for which there was a strong link to physical activity based on recent evidence reviews for physical activity guidelines.[14,15] An additional sensitivity analysis excluding the first 5 years of follow-up to reduce the risk of reverse causality was also conducted.[16] Statistical analyses were conducted in Stata (StataCorp LP).

Results

Final analyses were conducted in 292,559 apparently healthy participants with complete data on physical activity, outcomes, and covariates (see Supplementary Figure S1 in Supplementary Material [available online]) and without the following conditions/attributes at baseline: cancer, cardiovascular disease, chronic widespread pain, psychiatric problems, eating disorders, chronic neurological conditions, liver failure, and chronic obstructive pulmonary disease. In addition, we excluded participants who were underweight, pregnant, or unable to walk at baseline, as well as those with less than 2 years of follow-up. For both men and women, those who reported no physical activity were less likely to have a university degree, live with a partner, drink 3+ times a week, have a quality diet, and they were more likely to be a current smoker, have higher body fat percentages, and report more than 5 hours of screen time per day. They were also more likely to have a baseline diagnosis of hypertension, diabetes, and depression, and women with no reported physical activity were less likely to have had menopause, and more likely to use hormone replacement therapy (see Supplementary Tables S2 and S3 in Supplementary Material [available online]).

During a median follow-up of 11.0 years, 13,143 cancer cases were documented for men (9.2%, incidence density: 8.6/1000 person-years) and 10,255 for women (6.8%, 6.3/1000 person-years), 6488 deaths were recorded for men (4.5%, 4.1/1000 person-years) and 3739 for women (2.5%, 2.3/1000 person-years). Among men, the most common type of cancer was those in male genital organs (43.9%) and the most common type for women was breast cancer (40.8%). Physical activity related cancers accounted for 18.9% of all cancers in men and 46.7% in women (see Supplementary Table S4 in Supplementary Material [available online]).

For men, being in the "active" (600–1199 MET-min/wk) and "very active" (1200+ MET-min/wk) categories had a significant and inverse association with the transition from cancer-free to cancer (transition 1) and any nonzero level of physical activity was significantly associated with lower hazard of transitioning from cancer-free to death (transition 2). For women, any nonzero physical activity level was significantly associated with transition 2, but none of the physical activity levels was significantly associated with transition 1. None of the physical activity categories was associated with the transition from cancer to death (transition 3) in men or women (Table 1). The sensitivity analysis restricting to physical activity-related cancers revealed similar magnitudes of associations for women and weaker for men, particularly in transitions 1 and 3 (see Supplementary Table S5 in Supplementary Material [available online]).

LEFC at age 45 and 65 years was significantly higher in those who reported some physical activity than those who reported none (Table 2). At age 45, compared with men reporting no activity, those who were "insufficiently active," "active," and "very active" had a higher LEFC of 2.35 (1.01, 3.69), 2.46 (1.11, 3.81), and 2.76 (1.46, 4.06) years. These estimates were 1.44 (0.63, 2.25), 1.62 (0.81, 2.43), and 1.84 (1.06, 2.61) years for men at age 65. For women, compared with those who reported no activity, women who were "insufficiently active," "active," and "very active" had a higher LEFC of 1.09 (−0.21, 2.39), 1.42 (0.12, 2.72), and 1.59 (0.32, 2.86) years at age 45 and 1.25 (0.31, 2.19), 1.54 (0.61, 2.48), and 1.71 (0.80, 2.63) at age 65. Sensitivity analysis restricted to known physical activity-related cancers revealed similar magnitudes of associations (see Supplementary Table S6 in Supplementary Material [available online]). The sensitivity analysis excluding the first 5 years of follow-up also yielded similar estimates, with slightly weaker magnitude of associations for men, and stronger for women (see Supplementary Table S7 in Supplementary Material [available online]).

Discussion

Based on a large sample of men and women from the UK Biobank study, we found that doing physical activity equivalent to the

Table 1 Associations Between Physical Activity and Each Transition Based on Malignant Neoplasms[a]

	HR (95% CI) for transition 1: cancer-free to cancer	HR (95% CI) for transition 2: cancer-free to death	HR (95% CI) for transition 3: cancer to death
Men[b]			
Total n/n events	142,787/13,143	142,787/3253	13,098/3191
No activity (0 METs-min/wk)	1 (reference)	1 (reference)	1 (reference)
Inactive (<600 METs-min/wk)	0.91 (0.79 to 1.03)	0.70 (0.56 to 0.86)	1.02 (0.79 to 1.33)
Active (600–1200 METs-min/wk)	0.87 (0.76 to 0.99)	0.70 (0.56 to 0.86)	0.96 (0.74 to 1.24)
Very active (>1200 METs-min/wk)	0.85 (0.74 to 0.96)	0.67 (0.54 to 0.82)	0.87 (0.69 to 1.14)
Women[c]			
Total n/n events	149,772/10,255	149,772/1552	10,232/2165
No activity (0 METs-min/wk)	1 (reference)	1 (reference)	1 (reference)
Inactive (<600 METs-min/wk)	0.92 (0.79 to 1.09)	0.51 (0.38 to 0.68)	0.87 (0.63 to 1.21)
Active (600–1200 METs-min/wk)	0.89 (0.76 to 1.05)	0.45 (0.33 to 0.60)	0.81 (0.59 to 1.11)
Very active (>1200 METs-min/wk)	0.88 (0.75 to 1.03)	0.40 (0.30 to 0.52)	0.87 (0.64 to 1.18)

Abbreviations: CI, confidence interval; HR, hazard ratio; MET, metabolic equivalent.
[a]Malignant neoplasms do not include nonmelanoma skin cancer, benign neoplasms, in situ neoplasms, and neoplasms of uncertain or unknown behavior. [b]Models adjusted for age, deprivation, education, ethnicity, marital status, alcohol status, diet, smoking status, body fat, depression, diabetes, hypertension, and screen time. [c]Models adjusted for age, deprivation, education, ethnicity, marital status, alcohol status, diet, smoking status, body fat, depression, diabetes, hypertension, screen time, parity, hormone therapy replacement, menopause, age period, and oral contraceptive.

Table 2 Predicted LEFC by Physical Activity Category

	At 45 y old		At 65 y old	
	Marginal LEFC (95% CI)	Difference, y (95% CI)	Marginal LEFC (95% CI)	Difference, y (95% CI)
Men				
No activity (0 METs·min/wk)	30.14 (27.29 to 33.30)	Reference	18.46 (17.34 to 19.65)	Reference
Insufficiently active (<600 METs ·min/wk)	32.49 (29.43 to 35.88)	2.35 (1.01 to 3.69)	19.90 (18.87 to 20.99)	1.44 (0.63 to 2.25)
Active (600–1200 METs·min/wk)	32.61 (29.51 to 36.01)	2.46 (1.11 to 3.81)	20.08 (19.03 to 21.18)	1.62 (0.81 to 2.43)
Very active (>1200 METs·min/wk)	32.91 (29.80 to 36.35)	2.76 (1.46 to 4.06)	20.30 (19.26 to 21.39)	1.84 (1.06 to 2.61)
Women				
No activity (0 METs·min/wk)	44.16 (42.84 to 45.55)	Reference	22.24 (21.27 to 23.26)	Reference
Insufficiently active (<600 METs·min/wk)	45.26 (44.66 to 45.87)	1.09 (–0.21 to 2.39)	23.58 (23.17 to 24.00)	1.25 (0.31 to 2.19)
Active (600–1200 METs·min/wk)	45.60 (45.02 to 46.19)	1.42 (0.12 to 2.72)	23.89 (23.50 to 24.29)	1.54 (0.61 to 2.48)
Very active (>1200 METs·min/wk)	45.76 (45.26 to 46.28)	1.59 (0.32 to 2.86)	24.07 (23.75 to 24.40)	1.71 (0.80 to 2.63)

Abbreviations: CI, confidence interval; LEFC, life-expectancy free of cancer; MET, metabolic equivalent. Note: Predictions are conditional on reaching 100 years of age and made at the mean/median value for covariates included in the models.

amounts recommended by physical activity guidelines (150–300 minutes of weekly moderate-intensity physical activity)[14] was associated with nearly 2 more years of LEFC in women and more than 2 years in men. Even activities lower than the recommended levels were associated with a significant improvement in LEFC, and doing more than recommended levels was associated with a slight incremental improvement.

Our findings echo a recent smaller study on physical activity and LEFC which found similar LEFC estimates for selected cancer types.[9] Together, these studies reinforce the importance of physical activity in cancer prevention. The overall pattern of the association between physical activity and LEFC was similar to that identified for other health outcomes, such as all-cause mortality, where sizeable risk reduction is observed when moving people from "doing nothing" to "doing something."[15] Compared with other typical statistics reported, such as HRs, LEFC has the advantages of incorporating both morbidity with mortality and is a more interpretable statistic for the general public. Previous studies[17] calculating HRs for the associations between leisure-time physical activity and the risk of different cancer types have suggested generally modest effect sizes, similarly to our HRs, and that high amounts of physical activity may be needed to achieve significant risk reductions. Our findings, however, when using a multistate approach, suggest that the modest HRs may translate into relevant sufficient gains in LEFC, even at low amounts of physical activity. Nonetheless, the comparability of our findings with this prior evidence is limited, as our outcome was a composite of multiple cancer types. How the magnitude and pattern of associations between physical activity and LEFC vary across different cancer types warrants further investigation.

This study is subject to several limitations. Self-reported physical activity measured at one point in time is likely to bias the associations toward the null. Residual confounding due to unmeasured confounders or measurement errors could bias the associations in either direction. Additionally, our modeling approach, conditional on survival to 100 years, may be limited by the relatively short follow-up period and age of the sample at the end of the follow-up, which was below the average UK life expectancy of 79 years for men and 83 years for women.[18] Finally, the low participation rate of the UK Biobank study (<6%)[11] and missing data could lead to selection biases. However, it has been suggested that the lack of representativeness in the UK Biobank may not materially affect the associations of physical activity with disease incidence and mortality outcomes.[19,20]

Conclusions

Physical activity, even when performed below the recommended levels, adds cancer-free years to life. Considering the disease, and the social, and economic burden of cancer, physical activity should be promoted as an important strategy for cancer prevention.

Acknowledgments

Author Contributions: Sanchez-Lastra and del Pozo Cruz are joint first authors.

References

1. Kocarnik JM, Compton K, Dean FE, et al. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of disease study 2019. *JAMA Oncol*. 2022;8(3):420–444. doi:10.1001/JAMAONCOL.2021.6987
2. The Economic Burden of Cancer | The Cancer Atlas. 2024. Accessed February 15, 2024. https://canceratlas.cancer.org/taking-action/economic-burden/
3. Preventing Cancer. 2024. Accessed February 15, 2024. https://www.who.int/activities/preventing-cancer
4. Rock CL, Thomson C, Gansler T, et al. American cancer society guideline for diet and physical activity for cancer prevention. *CA Cancer J Clin*. 2020;70(4):245–271. doi:10.3322/CAAC.21591
5. Clinton SK, Giovannucci EL, Hursting SD. The world cancer research fund/American institute for cancer research third expert report on diet, nutrition, physical activity, and cancer: impact and future directions. *J Nutr*. 2020;150(4):663. doi:10.1093/JN/NXZ268
6. Cormie P, Atkinson M, Bucci L, et al. Clinical oncology society of Australia position statement on exercise in cancer care. *Med J Aust*. 2018;209(4):184–187. doi:10.5694/MJA18.00199
7. Ahmad AS, Ormiston-Smith N, Sasieni PD. Trends in the lifetime risk of developing cancer in Great Britain: comparison of risk for those born from 1930 to 1960. *Br J Cancer*. 2015;112(5):943–947. doi:10.1038/BJC.2014.606
8. Le-Rademacher JG, Peterson RA, Therneau TM, Sanford BL, Stone RM, Mandrekar SJ. Application of multi-state models in cancer clinical trials. *Clin Trials*. 2018;15(5):489–498. doi:10.1177/1740774518789098
9. Cuthbertson CC, Nichols HB, Tan X, et al. Associations of leisure-time physical activity and television viewing with life expectancy cancer-free at age 50: the ARIC study. *Cancer Epidemiol Biomarkers Prev*. 2020;29(12):2617. doi:10.1158/1055-9965.EPI-20-0870
10. Li Y, Schoufour J, Wang DD, et al. Healthy lifestyle and life expectancy free of cancer, cardiovascular disease, and type 2 diabetes: prospective cohort study. *Br Med J*. 2020;368:6669. doi:10.1136/BMJ.L6669
11. Sudlow C, Gallacher J, Allen N, et al. UK biobank: an open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med*. 2015;12(3):779. doi:10.1371/JOURNAL.PMED.1001779
12. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381–1395. doi:10.1249/01.MSS.0000078924.61453.FB
13. The IPAQ Group. *Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ)—Short and Long Forms Contents*. 2005.
14. World Health Organization. *Guidelines on Physical Activity and Sedentary Behaviour*. 2020.
15. 2018 Physical Activity Guidelines Advisory Committee. *2018 Physical Activity Guidelines Advisory Committee Scientific Report*. U.S. Department of Health and Human Services; 2018.
16. Tarp J, Hansen BH, Fagerland MW, Steene-Johannessen J, Anderssen SA, Ekelund U. Accelerometer-measured physical activity and sedentary time in a cohort of US adults followed for up to 13 years: the influence of removing early follow-up on associations with mortality. *Int J Behav Nutr Phys Act*. 2020;17(1):945. doi:10.1186/S12966-020-00945-4/FIGURES/2
17. Matthews CE, Moore SC, Arem H, et al. Amount and intensity of leisure-time physical activity and lower cancer risk. *J Clin Oncol*. 2020;38(7):686–698. doi:10.1200/JCO.19.02407/SUPPL_FILE/DS_JCO.19.02407.PDF
18. Office for National Statistics (ONS). National life tables—life expectancy in the UK: 2020 to 2022. 2024. Accessed November 8, 2024. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/bulletins/nationallifetablesunitedkingdom/2020to2022#cite-this-statistical-bulletin
19. Stamatakis E, Owen KB, Shepherd L, Drayton B, Hamer M, Bauman AE. Is cohort representativeness passé? Poststratified associations of lifestyle risk factors with mortality in the UK Biobank. *Epidemiology*. 2021;32(2):179–188. doi:10.1097/EDE.0000000000001316
20. Batty GD, Gale CR, Kivimäki M, Deary IJ, Bell S. Comparison of risk factor associations in UK Biobank against representative, general population based studies with conventional response rates: prospective cohort study and individual participant meta-analysis. *Br Med J*. 2020;368:131. doi:10.1136/BMJ.M131