Welcome to a new journal in exercise and cancer

Alejandro Lucia . *Research Group in Physical Activity and Health. Faculty of Physical Activity and Sports Sciences. European University of Madrid. Spain.*

Dear Editor:

Traditionally, patients with cancer were told to rest as much as possible and to avoid physical activity — not to mention strenuous exercise, which was not even a question. Yet an exponentially growing number of studies since the end of the last century have shown beneficial effects of not only regular, moderate physical activity but also supervised (sometimes even intense) exercise in the cancer continuum. Notably, for attenuating treatment-related toxicities and side effects. Thus, the paradigm has now shifted to the concept of "*exercise is medicine*", with leading world experts advocating that "*all people living with and beyond cancer can be as active as is possible for them*" (Schmitz et al., 2019).

The initial scientific work on exercise intervention during cancer treatment was published in 1989 by Winningham and co-workers. These authors showed the benefits of aerobic exercise training performed during chemotherapy on the body composition of women with breast cancer (Winningham et al., 1989). The same group also documented benefits on these patients' functional capacity (MacVicar et al., 1989), as well as on their self-reports of nausea (MacVicar et al., 1988). Some years later, before the start of the new

Corresponding author. *Facultad de Ciencias del Deporte. Universidad Europea de Madrid. Madrid, Spain.*
E-mail: alejandro.lucia@universidadeuropea.es
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century, Dimeo *et al*. published the first randomized controlled trial showing that exercise can attenuate chemotherapy-related toxicities (Dimeo et al., 1997). This pioneering effort was followed by an exponentially growing number of trials corroborating and expanding the aforementioned results in numerous types of malignancies. As a result, several prestigious organizations have now launched exercise recommendations for patients living with and beyond cancer. Notably, according to an expert international panel from the American College of Sports Medicine, "*there is sufficient evidence to support the efficacy of specific doses of exercise training to address cancer-related health outcomes*" including fatigue, physical function, anxiety, depressive symptoms, as well as health-related quality of life (Campbell et al., 2019).

Regular physical activity is also associated with lower cancer incidence (Ahmadi et al., 2022; Matthews et al., 2020), recurrence (Morishita et al., 2020), and mortality (Morishita et al., 2020; Arem et al., 2015). Importantly, this protective association is largely independent of major confounders (such as body mass index or smoking status) (Moore et al., 2016) and is potentially dose-response dependent, with a benefit threshold for mortality at approximately 3-5 times the minimum World Health Organization-determined dose and no excess risk at 10+ times the minimum dose (Arem et al., 2015). In fact, the first proof-of-concept biological evidence for a protective association between physical exercise (even at very high doses) and cancer was reported as early as in 1944 by Rush and Kline in albino mice with fibrosarcoma (Rusch et al., 1944). These visionary scientists showed that forced exercise applied for 2 or 16 hours/day delayed tumour growth rate by ~34% and ~25%, respectively, compared to controls (Rusch et al., 1944). Since then, a growing number of studies has attempted to identify the mechanisms underlying the potential antitumorigenic effects of exercise or physical activity.

The stimulation of immune function is a strong candidate to explain the potential anticancer effects of both *acute* and *regular* exercise (Rusch et al., 1944). Notably, the muscle modulates immune function through the release of 'myokines', such as interleukin (IL)6 and mainly IL7 and IL15. These signalling moieties can stimulate lymphocyte mobilization to tumours (IL6) or improve the proliferation and homeostasis of a major immune effector against tumours, $CD8^+$ T lymphocytes (IL7 and IL15) (Rusch et al., 1944). Furthermore, during each acute exercise session (*e.g.*, cycle-ergometer exercise at moderate-high intensities for up to 1 hour) and the subsequent post-exercise window (a few hours) adrenaline-stimulated immune effectors with a strong cytotoxic effect against nascent tumours [natural killer (NK) cells and the aforementioned $CD8^+$ T lymphocytes] are released in high amounts (*i.e.*, two or threefold higher compared to baseline) to the bloodstream(Rusch et al., 1944). These exercise-primed immune subsets are potentially able to infiltrate ('heat') tumours, at least after the accumulation of repeated acute bouts of exercise — that is, with *regular* exercise (Rusch et al., 1944).

According to scientific evidence, *physical exercise is beneficial for people with cancer*. As such, we believe that launching a new scientific journal solely focused on this field is always good news. Especially to attempt answering the numerous questions that remain open. These include, among numerous other unsolved issues: adequate identification and reporting of potential adverse effects of exercise interventions (as it is done in pharma trials); how to implement exercise interventions in *oldest old* patients (*i.e.*, those aged 80 years and above, who unfortunately represent the 'great forgotten' population segment in the medical literature); or how to close the gap between preclinical evidence (where exercise delays tumour growth in many animal models, including in the context of aggressive cancers) and the real clinical world (where exercise is unlikely to delay the growth of very aggressive malignancies). Furthermore, the biological mechanisms behind the potential exercise effects in the fascinating tumour microenvironment — a heterogeneous and continuously evolving universe of tumour and nontumor cells, including both

immunosuppressive and anticancer effectors — are awaiting to be studied in depth, including at the granular (single-cell) level. The task ahead is enormous.

Keywords: Physical exercise, Physical activity, Exercise, Cancer, Cancer prevention, Cancer treatments, Cancer survivors, Psychology, Sport medicine.

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REFERENCES

Ahmadi, M. N., Clare, P. J., Katzmarzyk, P. T., del Pozo Cruz, B., Lee, I. M., & Stamatakis, E. (2022). Vigorous physical activity, incident heart disease, and cancer: how little is enough? European Heart Journal, 43(46), 4801–4814. https://doi.org/10.1093/eurheartj/ehac572

Arem, H., Moore, S. C., Patel, A., Hartge, P., Berrington de Gonzalez, A., Visvanathan, K., Campbell, P. T., Freedman, M., Weiderpass, E., Adami, H. O., Linet, M. S., Lee, I.-M., & Matthews, C. E. (2015). Leisure Time Physical Activity and Mortality: A Detailed Pooled Analysis of the Dose-Response Relationship. JAMA Internal Medicine, 175(6), 959–967. https://doi.org/10.1001/jamainternmed.2015.0533

Campbell, K. L., Winters-Stone, K. M., Wiskemann, J., May, A. M., Schwartz, A. L., Courneya, K. S., Zucker, D. S., Matthews, C. E., Ligibel, J. A., Gerber, L. H., Morris, G. S., Patel, A. V, Hue, T. F., Perna, F. M., & Schmitz, K. H. (2019). Exercise Guidelines for Cancer Survivors: Consensus Statement from International Multidisciplinary Roundtable. Medicine & Science in Sports & Exercise, 51(11). https://doi.org/10.1249/MSS.0000000000002116

Dimeo, F., Fetscher, S., Lange, W., Mertelsmann, R., & Keul, J. (1997). Effects of Aerobic Exercise on the Physical Performance and Incidence of Treatment-Related Complications After High-Dose Chemotherapy. Blood, 90(9), 3390–3394. https://doi.org/10.1182/blood.V90.9.3390

Fiuza-Luces, C., Valenzuela, P. L., Gálvez, B. G., Ramírez, M., López-Soto, A., Simpson, R. J., & Lucia, A. (2023). The effect of physical exercise on anticancer immunity. Nature Reviews Immunology. https://doi.org/10.1038/s41577-023-00943-0

Friedenreich, C. M., Stone, C. R., Cheung, W. Y., & Hayes, S. C. (2020). Physical Activity and Mortality in Cancer Survivors: A Systematic Review and Meta-Analysis. JNCI Cancer Spectrum, 4(1), pkz080. https://doi.org/10.1093/jncics/pkz080

MacVicar, M. L., MacVicar, M. G. (1988). The effect of aerobic exercise on patient reports of nausea. Oncol Nurs Forum,15:447-50.

MacVicar, M. G., Winningham, M. L., & Nickel, J. L. (1989). Effects of Aerobic Interval Training on Cancer Patients' Functional Capacity. Nursing Research, 38(6). https://doi.org/10.1097/00006199-198911000-00007

Matthews, C. E., Moore, S. C., Arem, H., Cook, M. B., Trabert, B., Håkansson, N., Larsson, S. C., Wolk, A., Gapstur, S. M., Lynch, B. M., Milne, R. L., Freedman, N. D., Huang, W.-Y., Berrington de Gonzalez, A., Kitahara, C. M., Linet, M. S., Shiroma, E. J., Sandin, S., Patel, A. V, & Lee, I.-M. (2019). Amount and Intensity of Leisure-Time Physical Activity and Lower Cancer Risk. Journal of Clinical Oncology, 38(7), 686–697. https://doi.org/10.1200/JCO.19.02407

Moore, S. C., Lee, I.-M., Weiderpass, E., Campbell, P. T., Sampson, J. N., Kitahara, C. M., Keadle, S. K., Arem, H., Berrington de Gonzalez, A., Hartge, P., Adami, H.-O., Blair, C. K., Borch, K. B., Boyd, E.,

Check, D. P., Fournier, A., Freedman, N. D., Gunter, M., Johannson, M., … Patel, A. V. (2016). Association of Leisure-Time Physical Activity With Risk of 26 Types of Cancer in 1.44 Million Adults. JAMA Internal Medicine, 176(6), 816–825. https://doi.org/10.1001/jamainternmed.2016.1548

Morishita, S., Hamaue, Y., Fukushima, T., Tanaka, T., Fu, J. B., & Nakano, J. (2020). Effect of Exercise on Mortality and Recurrence in Patients With Cancer: A Systematic Review and Meta-Analysis. Integrative Cancer Therapies, 19, 1534735420917462. https://doi.org/10.1177/1534735420917462

Rusch, H. P., Kline, B. E. (1944). The Effect of Exercise on the Growth of a Mouse Tumor. Cancer Res., 4:116-118.

Schmitz, K. H., Campbell, A. M., Stuiver, M. M., Pinto, B. M., Schwartz, A. L., Morris, G. S., Ligibel, J. A., Cheville, A., Galvão, D. A., Alfano, C. M., Patel, A. V, Hue, T., Gerber, L. H., Sallis, R., Gusani, N. J., Stout, N. L., Chan, L., Flowers, F., Doyle, C., … Matthews, C. E. (2019). Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. CA: A Cancer Journal for Clinicians, 69(6), 468–484. https://doi.org/https://doi.org/10.3322/caac.21579

Winningham, M. L., MacVicar, M. G., Bondoc, M., Anderson, J. I., Minton, J. P. (1989). Effect of aerobic exercise on body weight and composition in patients with breast cancer on adjuvant chemotherapy. Oncol Nurs Forum, 16:683-9.

