Available online at www.sciencedirect.com

ScienceDirect

Journal of Sport and Health Science 12 (2023) 726−738

Review

Comparative effects of different types of exercise on health-related quality of life during and after active cancer treatment: A systematic review and network meta-analysis

Vicente Martínez-Vizcaíno [a,b], Iván Cavero-Redondo [b,*], Sara Reina-Gutiérrez [a], Luis Gracia-Marco [c], José J. Gil-Cosano [c], Bruno Bizzozero-Peroni [a,d], Fernando Rodriguez-Artalejo [e,f,g], Esther Ubago-Guisado [g,h,i]

[a] *Universidad de Castilla-La Mancha, Health and Social Research Center, Cuenca 16071, Spain*
[b] *Facultad de Ciencias de la Salud, Universidad Autónoma de Chile, Talca 3460000, Chile*
[c] *PROFITH (PROmoting FITness and Health through physical activity) Research Group, Department of Physical Education and Sports, Faculty of Sport Sciences, Sport and Health University Research Institute (iMUDS), University of Granada, Granada 18012, Spain*
[d] *Higher Institute for Physical Education, Universidad de la República, Rivera 40000, Uruguay*
[e] *Department of Preventive Medicine and Public Health, School of Medicine, Universidad Autónoma de Madrid, Madrid 28029, Spain*
[f] *IdiPaz (Instituto de Investigación Sanitaria Hospital Universitario La Paz), Madrid 28029, Spain*
[g] *Epidemiology and Control of Chronic Diseases, CIBER of Epidemiology and Public Health (CIBERESP), Madrid 28029, Spain*
[h] *Cancer Registry of Granada, Escuela Andaluza de Salud Pública, Granada 18011, Spain*
[i] *Cancer Epidemiology Group, Instituto de Investigación Biosanitaria, Granada 18012, Spain*

Received 12 July 2022; revised 22 October 2022; accepted 28 November 2022
Available online 3 February 2023

Abstract

Background: The positive influence of most types of exercise has been reported repeatedly, but what the most effective exercise approaches are for improving health-related quality of life (HRQoL) in people with cancer remains unknown. The aim of this systematic review and network meta-analysis was to synthesize the evidence from intervention studies to assess the effects of different types of exercise on HRQoL during and after cancer treatment.

Methods: MEDLINE, SPORTDiscus, the Cochrane Library, Web of Science, and Scopus were searched for randomized controlled trials aimed at testing the effects of exercise interventions meant to improve HRQoL in people with cancer. Separate analyses were conducted for HRQoL as measured by general and cancer-specific questionnaires. We also evaluated whether the effects of exercise were different during and after cancer treatment in both the physical and mental HRQoL domains.

Results: In total, 93 studies involving 7435 people with cancer were included. Network effect size estimates comparing exercise intervention *vs.* usual care were significant for combined exercise (0.35, 95% confidence interval (95%CI): 0.14−0.56) for HRQoL as measured by general questionnaires, and for combined (0.31, 95%CI: 0.13−0.48), mind−body exercise (0.54, 95%CI: 0.18−0.89), and walking (0.39, 95%CI: 0.04−0.74) for HRQoL as measured by cancer-specific questionnaires.

Conclusion: Exercise programs combining aerobic and resistance training can be recommended to improve HRQoL during and after cancer treatment. The scarcity and heterogeneity of these studies prevents us from making recommendations about other exercise modalities due to insufficient evidence.

Keywords: Cancer; Exercise; HRQoL; Physical activity

1. Introduction

Recent estimates predict that more than 28 million new cancer cases will occur in 2040 worldwide, which represents a 47% increase from 19.3 million cases in 2020.[1] In parallel

Peer review under responsibility of Shanghai University of Sport.
* Corresponding author.
E-mail address: Ivan.Cavero@uclm.es (I. Cavero-Redondo).

https://doi.org/10.1016/j.jshs.2023.01.002
Cite this article: Martínez-Vizcaíno V, Cavero-Redondo I, Reina-Gutiérrez S, et al. Comparative effects of different types of exercise on health-related quality of life during and after active cancer treatment: A systematic review and network meta-analysis. *J Sport Health Sci* 2023;12:726−38.

with this increasing incidence, the number of people living with cancer is expected to increase due to earlier diagnoses and treatment improvements, the decline in cardiovascular mortality, and the ageing of the population.[2] Maintaining the functional capacity and overall health-related quality of life (HRQoL) of cancer survivors will challenge health and social services.

HRQoL is a construct that reflects the perceptions of patients regarding their well-being, which is mainly determined by their social, physical, and psychological functioning.[3] Cancer negatively impacts all dimensions of the HRQoL of patients not only during treatment and the early years after diagnosis but also over the long term.[4] Moreover, cancer therapies are often associated with direct adverse effects such as cardiotoxicity, which greatly impairs the cardiorespiratory capacity, but there are also some indirect effects, such as deconditioning and weight gain. As a consequence, both the direct and indirect effects of treatments further undermine the HRQoL of cancer patients.[5] Therefore, strategies to mitigate the negative impacts of cancer in each of its dimensions are important from a clinical and public health perspective.

Among such strategies, exercise is the main nonpharmacological intervention suggested for producing improvements in the different dimensions of HRQoL. It has been reported that exercise may attenuate the development of metastases,[6] enhance the immune system by fostering natural killer cells,[7] decrease low-grade inflammation and insulin resistance via the release of myokines triggered by the contraction of skeletal muscle,[8] improve cardiorespiratory fitness,[9] and enhance the effects of systemic therapies by improving tumoral microenvironment perfusion and thereby mitigating the aggressiveness of the cancer phenotype.[10]

There is growing interest in studying the effects of exercise interventions on the physical, psychological, and social dimensions of HRQoL. Several systematic reviews have documented improvements in cardiorespiratory fitness, fatigue, strength, physical function,[10,11] and psychological outcomes (depression, anxiety, and sleep quality).[12] Likewise, a systematic review of systematic reviews concluded that, for all cancer types, exercise before, during, and after treatment elicits benefits with respect to a wide variety of adverse health consequences.[12] Finally, in 2018, an international multidisciplinary consensus roundtable was convened to update available evidence on the benefits of physical activity and exercise for patients with cancer. They recommended exercise prescription during and after treatment as a therapeutic strategy to mitigate the adverse effects of cancer diagnosis and treatment, including decrease in physical function, greater levels of fatigue, anxiety, and depressive symptoms, and lower HRQoL.[13] Still, although a positive influence has been reported for most exercise modalities, it remains unknown what the most effective exercise approaches for improving the HRQoL of people with cancer are.

We conducted this systematic review and network meta-analysis (NMA) to synthesize the evidence provided by intervention studies aimed at assessing the effects of different types of exercise on HRQoL during and after cancer treatment. We distinguish between studies that assess HRQoL with cancer-specific *vs.* general questionnaires as well as between the physical and mental domains of HRQoL. NMA techniques allow us to comparatively evaluate the effects of different types of exercise on HRQoL in people with cancer.

2. Methods

This NMA was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-analysis Protocols statement extension for PRISMA−NMA guidelines[14] (Supplementary Table 1) and conducted following the Cochrane Handbook for Systematic Reviews of Interventions recommendations.[15] This systematic review and NMA have been registered in International Prospective Register of Systematic Reviews (PROSPERO) (registration number: CRD42019125028), and its protocol has been published previously.[16] Approval was not requested from any institutional ethics research committee because this study did not include individual patient data and all studies were published previously.

2.1. Data sources and searches

The systematic search for studies was carried out through 5 databases (MEDLINE (via PubMed), SPORTDiscus, the Cochrane Library, Web of Science, and Scopus) from their inception to September 16, 2022 (Supplementary Tables 2 and 3). In the MEDLINE and Embase databases, the search was conducted using controlled (MeSH and Emtree vocabulary) and not controlled vocabulary. The search strategy was structured according to the Peer Review of Electronic Search Strategies 2015 guidelines.[17]

To perform the search, the following keywords were used: (cancer OR tumour OR tumor OR oncology OR chemotherapy OR radiotherapy) AND (exercise OR "physical activity" OR aerobic OR resistance OR anaerobic OR muscular OR strength OR cardiovascular OR flexibility OR balance) AND ("quality of life" OR "QoL" OR "health related quality of life" OR "HRQoL" OR "life quality"). Furthermore, we searched for relevant studies in the reference lists of included articles and previous systematic reviews or meta-analyses, as well as using ClinicalTrials.gov, the World Health Organization International Clinical Trials Registry Platform, and the International Standard Randomized Controlled Trial Number Registry for all registered clinical trials and randomized controlled trials (RCTs). The study records were managed using Covidence software (Level 4; Covidence, Melbourne, VIC, Australia).

2.2. Eligibility

RCT studies concerning the effects of physical exercise on the HRQoL of cancer survivors were included in the meta-analysis. The inclusion criteria were as follows: (a) population: cancer patients (during treatment) and/or cancer survivors (after treatment) over 18 years of age; (b) intervention: type of exercise (aerobic, resistance training, combined exercise (aerobic and resistance), anaerobic, walking, stretching, and mind−body exercises (pilates, Tai Chi, and yoga)); (c) outcome: quality of life measured by general or cancer-specific questionnaires; and (d) comparison: inclusion of 2 or more groups (i.e., exercise *vs.* control group).

The exclusion criteria included: (a) quasi-experimental studies not including a comparison group; (b) studies of interventions combining exercise with diet or drug treatments; and (c) studies not written in English or Spanish (authors' languages).

2.3. Study selection and data extraction

The selection of studies was independently performed by 2 researchers (VMV and EUG). When agreement was not reached between them, a third reviewer (ICR) was consulted. The agreement rate between reviewers was 0.92 (calculated using κ statistics).

The following data were independently collected from each study that met the inclusion criteria: (a) first author and year of publication, (b) country of the study where data were collected, (c) design, (d) sample characteristics (age and sample size), (e) cancer characteristics (cancer type and stage of treatment), (f) outcome measures (baseline and/or follow-up values), and (g) intervention characteristics (type of exercise, length, frequency). When a lack of information was detected in any of the included studies, we contacted the authors through e-mail.

2.3.1. Classification as "during" or "after" cancer treatment

Most studies addressing the effects of exercise on HRQoL in cancer patients distinguish between benefits achieved during and after treatment.[11] Therefore, this study distinguishes between analyses that include patients receiving chemotherapy or radiotherapy as the initial cancer treatment or as treatment in the presence of metastasis or cancer recurrence, classifying these as "during", and those studies that include patients currently not on chemotherapy or radiotherapy, which were categorized as "after". Studies including both types of patients were classified as "both"; studies including patients receiving androgen suppression therapy without chemotherapy or radiotherapy were defined as "after".

2.3.2. Missing data imputation

For HRQoL (continuous variable) values, means and standard deviations were extracted when available. When standard deviations were not reported, they were calculated from standard errors, confidence intervals, or other measures. When the sample size was not provided in the analysis table, it was extracted from the descriptive statistics. If HRQoL data were missing, we used the number of individuals who met the response criteria as defined by the study's authors.[18]

2.3.3. Categorization of available evidence

Physical exercise refers to the subset of planned and repetitive physical activity aimed at improving physical fitness and, thus, maintaining a good health status.[19] The exercise interventions depicted in this NMA were classified as aerobic exercise (including interventions aimed at increasing heart rate and energy expenditure), resistance training (interventions aimed at increasing muscle strength and muscle power), walking, combined exercise (aerobic exercise and resistance training), stretching, and mind−body exercises (i.e., pilates, Tai Chi, and yoga; modalities of exercise that combine body movement, mental focus, and controlled breathing for improved strength, balance, and flexibility).

2.3.4. Risk of bias assessment

Once the information about the authors, dates, and sources of each included manuscript was blinded, 2 researchers (VMV and EUG) independently assessed the risk of bias. Disagreements were resolved by a third reviewer (ICR). The agreement rate between reviewers was 0.90 (calculated using κ statistics).

The risk of bias of the RCTs was assessed using the Cochrane Collaboration's tool for assessing risk of bias (RoB2).[20] This tool evaluates the risk of bias according to 5 domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Overall, there is a "low risk of bias" if all domains are classified as "low risk", there are "some concerns" if at least 1 domain is rated as "some concern", and there is a "high risk of bias" if at least 1 domain is rated as "high risk" or if several domains are rated as "some concerns".

2.3.5. Grading the quality of evidence

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) tool was used to evaluate the quality of the evidence and make recommendations.[21] Each outcome obtained a high, moderate, low, or very low evidence value, depending on the design of the studies, risk of bias, inconsistency, indirect evidence, imprecision, and publication bias. The GRADE tool was used only for the pairwise meta-analysis.

2.4. Data synthesis and statistical analysis

The included studies were summarized qualitatively in an *ad hoc* table describing the types of direct and indirect comparisons. Our systematic review and NMA were carried out in accordance with the PRISMA−NMA statement[14] under a frequentist perspective in 5 steps. Separate analyses were conducted for HRQoL as measured by general and cancer-specific questionnaires. To display the relative accumulated available evidence on each modality of exercise, we designed a network geometry graph in which the nodes represent each type of exercise intervention and the edges correspond to direct head-to-head comparisons between interventions. The size of the nodes correlates to the number of participants for each type of exercise, and the thickness of the edges is proportional to the number of studies accumulated in trials that directly compare each pair of physical exercise interventions; the dashed lines represent indirect comparisons between any 2 interventions.[22] Second, to verify that the effects of direct interventions were consistent with those of indirect comparisons, we utilized the Wald test and, because of its low statistical power, used side-splitting as an additional consistency assessment. Third, we conducted pairwise meta-analysis for direct and indirect comparisons between interventions and control/non-interventions using the random effects DerSimonian−Laird method.[23] For this analysis we used the standardized mean difference (as effect size (ES)) between the change in HRQoL of intervention and control/non-intervention groups. We conducted analyses for effects on HRQoL during and after active treatment separately, and when possible, we analyzed physical and mental domains of HRQoL separately as well. For this analysis, we examined statistical heterogeneity by calculating the I^2 statistic, the values of which were considered not important (0%−40%), moderate (30%−60%), substantial (50%−90%), or considerable (75%−100%).[15] In addition, to determine the size and clinical relevance of heterogeneity, we calculated the τ^2 statistic; its degree of clinical relevance of heterogeneity was estimated as low when values were lower than 0.14, moderate when values ranged from 0.14 to 0.40, and substantial when values were higher than 0.40.[24] Fourth, the pooled effect of each intervention was performed using a frequentist approach of the NMA. Fifth, for the transitivity assessment, we used sensitivity to check that all the participants in the studies included in the NMA had the same baseline distribution (on average) of effect. Sensitivity analysis (systematic reanalysis while removing studies one at a time) was conducted to assess the robustness of the summary estimates. Lastly, once the ES estimates of the effects of exercise interventions were calculated, we ranked the interventions to identify superiority and presented them graphically using rankograms. Additionally, we estimated the surface under the cumulative ranking (SUCRA) for each intervention. SUCRA involves the assignment of a numerical value between 0 and 1 to simplify the classification of each intervention in the rankogram. The best intervention obtained a SUCRA value closest to 1, and the worst intervention obtained a value closest to 0.[22,25] We also calculated rank exercise modalities using the p score as the probability of being, comparatively to others, the best treatment option.[26]

Finally, publication bias was assessed through visual inspection of the funnel plots as well as by the method proposed by Egger.[27] Pairwise meta-analysis, frequentist NMA, and production of network graphs and resulting figures were performed using the network and network graph packages in Stata 16.0 (Stata Corp., College Station, TX, USA).

2.5. Data sharing

After the publication of this article, the full dataset will be available online in Mendeley Data, a repository of research data that allows the assignment of a permanent digital object identifier in such a way that the data can be easily referenced (doi: 10.17632/2c4y6k32g5.1).

2.6. Modifications to the initial protocol

Although the protocol initially included The Quality Assessment of Systematic Reviews and Meta-analyses of the National Heart, Lung, and Blood Institute for the assessment of the risk of bias, as the studies included are all clinical trials, this NMA followed the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions and used the RoB2 tool for the assessment of the risk of bias.

3. Results

3.1. Study characteristics

A total of 93 studies[28−120] were included in this NMA (Fig. 1). The characteristics of the included studies are shown in Supplementary Table 4. All included studies were RCTs. The most frequently reported type of exercise was combined exercise ($n = 39$ interventions), followed by resistance training ($n = 22$ interventions), aerobic exercise ($n = 19$ interventions), walking ($n = 10$ interventions), and mind−body exercises ($n = 10$ interventions). Furthermore, 8 studies had 3 arms (2 interventions and 1 control). In total, 3697 participants were randomly allocated to an exercise intervention and 3466 were assigned to a control group. Participants in exercise intervention groups and control groups showed no differences in age or baseline QoL scores.

3.2. Risk of bias and GRADE

The overall risk of bias for RCTs showed some concerns, especially due to the high risk of bias in most included studies. Specifically, for measurement of outcome and missing outcome data, respectively, 92 (98.9%) and 90 (96.8%) studies were scored as low bias; for randomization process and deviations from intentional interventions, respectively, 77 (82.8%) and 70 (75.3%) studies showed a low risk of bias (Supplementary Table 5).

The quality of evidence of each pairwise comparison was evaluated using the GRADE system. The quality of evidence and recommendations was classified as low in 82 peer

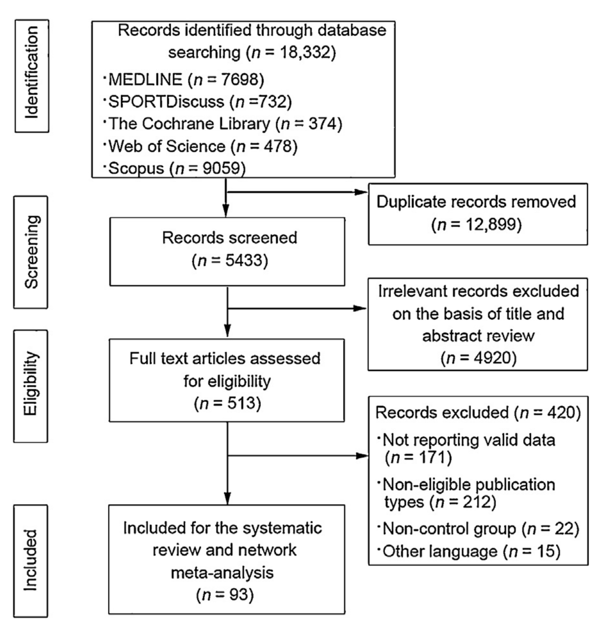

Fig. 1. Preferred Reporting Items for Systematic Reviews flowchart.

comparisons (73.9%) and very low in 29 comparisons (26.1%) (Supplementary Table 6).

3.2.1. Exercise effects on HRQoL as measured by general and cancer-specific questionnaires

Network maps of included comparisons testing the effects of different exercise modalities on HRQoL as measured by general and cancer-specific questionnaires are shown in Fig. 2. Table 1 shows the pairwise (upper diagonal) and NMA (lower diagonal) ES estimates. In the pairwise analyses, compared to the control, only the ES for combined exercise was significant (0.45, 95% confidence interval (95%CI): 0.16−0.74) for HRQoL as measured by general questionnaires; also significant were combined exercise (0.20, 95%CI: 0.10−0.29), aerobic exercise (0.14, 95%CI: 0.01−0.27), resistance training (0.17, 95%CI: 0.04−0.29), and walking (0.32, 95%CI: 0.09−0.55) for HRQoL as measured by cancer-specific questionnaires. Network ES estimates were significant for combined exercise (0.45, 95%CI: 0.16−0.74) for HRQoL as measured by general questionnaires and for combined exercise (0.31, 95%CI: 0.13−0.48), mind−body exercise (0.54, 95%CI: 0.18−0.89), and walking (0.39, 95%CI: 0.04−0.74) for HRQoL as measured by cancer-specific questionnaires. Risk of bias and indirectness contributions in the network analyses were assessed with the Confidence in NMA Web application and are presented in Supplementary Figs. 1−4.

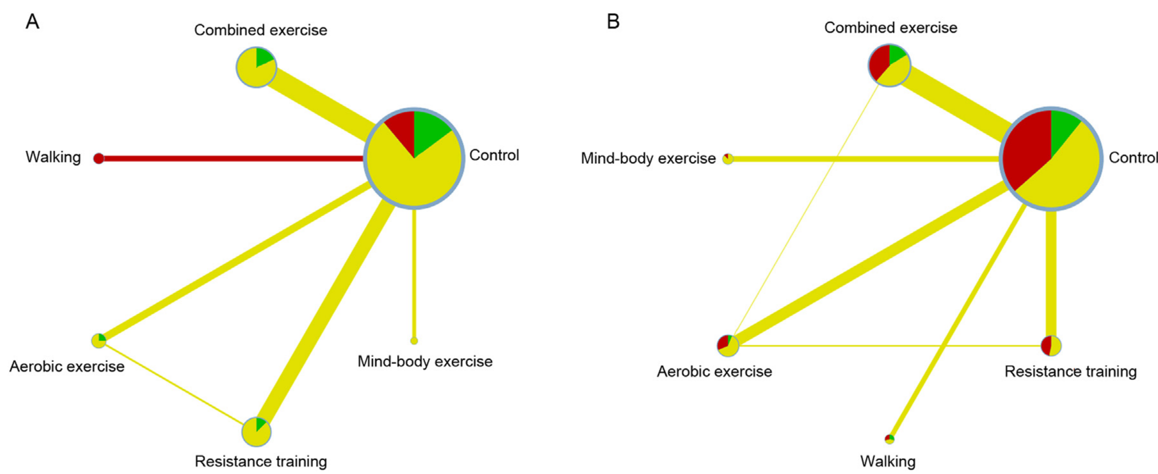

Fig. 2. Network of available comparisons between exercises interventions on quality of life as measured by (A) general questionnaires and (B) cancer-specific questionnaires. The size of the node is proportional to number of trial participants, and thickness of the continuous line connecting nodes is proportional to number of participants randomized in trials directly comparing the 2 treatments. Colored areas correspond with the proportion of studies for each node with respect to risk of bias assessment as follows: green for low risk, yellow for some concerns, and red for high risk of bias. The color of the lines corresponds with the average of the risk of bias assessment of the studies directly comparing the 2 interventions.

Table 1
League table of pooled effect sizes for general and cancer-specific questionnaires on quality of life.

A. Quality of life as measured by general questionnaires

Control	0.12 (−0.12 to 0.35)	0.12 (−0.01 to 0.25)	0.35 (−0.17 to 0.88)	0.09 (−0.16 to 0.35)	**0.45 (0.16 to 0.74)**
0.15 (−0.22 to 0.52)	Walking	na	na	na	na
0.24 (0.00 to 0.49)	0.09 (−0.35 to 0.54)	Resistance training	na	−0.10 (−0.43 to 0.23)	na
0.58 (−0.39 to 1.55)	0.43 (−0.61 to 1.47)	0.34 (−0.66 to 1.34)	Mind−body exercise	na	na
0.20 (−0.18 to 0.58)	0.05 (−0.48 to 0.58)	−0.05 (−0.49 to 0.40)	−0.38 (−1.42 to 0.66)	Aerobic exercise	na
0.35 (0.14 to 0.56)	0.20 (−0.22 to 0.62)	0.11 (−0.21 to 0.42)	−0.23 (−1.22 to 0.76)	0.15 (−0.28 to 0.59)	Combined exercise

B. Quality of life as measured by cancer-specific questionnaires

Control	**0.32 (0.09 to 0.55)**	**0.17 (0.04 to 0.29)**	0.40 (−0.17 to 0.97)	**0.14 (0.01 to 0.27)**	**0.20 (0.10 to 0.29)**
0.39 (0.04 to 0.74)	Walking	na	na	na	na
0.25 (−0.01 to 0.50)	−0.14 (−0.58 to 0.29)	Resistance training	na	0.06 (−0.30 to 0.42)	na
0.54 (0.18 to 0.89)	0.15 (−0.36 to 0.65)	0.29 (−0.15 to 0.73)	Mind−body exercise	na	na
0.20 (−0.05, 0.45)	−0.19 (−0.62 to 0.25)	−0.05 (−0.38 to 0.29)	−0.34 (−0.77 to 0.10)	Aerobic exercise	0.05 (−0.57 to 0.67)
0.31 (0.13 to 0.48)	−0.08 (−0.48 to 0.31)	0.06 (−0.25 to 0.37)	−0.23 (−0.63 to 0.17)	0.11 (−0.20 to 0.41)	Combined exercise

Notes: Data are effect sizes (95% confidence intervals). Effect sizes in bold are statistically significant. Positive effect sizes mean that the first intervention improves quality of life compared to the second intervention. Upper right triangle gives pooled effect sizes from pairwise comparisons (column intervention relative to row); lower left triangle gives pooled effect sizes from the network meta-analysis (row intervention relative to column).
Abbreviation: na = not available.

3.2.2. Exercise during and after treatment

Table 2 shows ES estimates for HRQoL during and after treatment as measured by general and specific questionnaires. During treatment, in the pairwise analyses (upper diagonal), compared to the control, combined exercise and aerobic exercise showed significant ES (0.56, 95%CI: 0.20−0.92 and 0.40, 95%CI: 0.02−0.78, respectively) for HRQoL as measured by general questionnaires; combined exercise, aerobic exercise, and resistance training also showed significant ESs (0.15, 95%CI: 0.03−0.27; 0.22, 95%CI: 0.05−0.40; and 0.15, 95%CI: 0.01−0.29, respectively) for HRQoL as measured by cancer-specific questionnaires. Network ES estimates were significant for combined exercise (0.44, 95%CI: 0.27−0.61) for HRQoL as measured by general questionnaires and for combined exercise (0.32, 95%CI: 0.03−0.61) and mind−body exercise (0.92, 95%CI: 0.34−1.51) for HRQoL as measured by cancer-specific questionnaires.

After treatment, no intervention showed a significant ES when general HRQoL questionnaires were used. When cancer-specific questionnaires were used, combined exercise and walking resulted in a significant effect in both pairwise (0.28, 95%CI: 0.12−0.44 and 0.26, 95%CI: 0.03−0.49, respectively) and network analyses (0.41, 95%CI: 0.22−0.60 and 0.35, 95%CI: 0.01−0.68, respectively).

3.2.3. Exercise effects on physical and mental domains

When the analyses were performed separately for the physical and mental domains, only combined exercise showed a statistically significant ES in both pairwise and network analyses (0.52, 95%CI: 0.23−0.82 for the physical domain and 0.59, 95%CI: 0.24−0.95 for the mental domain) (Table 3).

3.3. Probabilities

Mind−body exercise showed a higher probability of being the best treatment (62.8% for HRQoL measured by general questionnaires and 65.1% for HRQoL measured by cancer-specific questionnaire). The SUCRA value was higher for mind−body exercise for HRQoL measured by general questionnaires (77.0%) and for mind−body exercise for HRQoL measured by cancer-specific questionnaires (88.4%) (Fig. 3).

Table 2
League table of pooled effect sizes for general and cancer-specific questionnaires on quality of life by time period.

A. Quality of life as measured by general questionnaires (during treatment)

Control	0.41 (−0.03 to 0.84)	0.11 (−0.18 to 0.39)	0.35 (−0.17 to 0.88)	**0.40 (0.02 to 0.78)**	**0.56 (0.20 to 0.92)**
0.60 (−0.08 to1.28)	Walking	na	na	na	na
0.21 (−0.21 to 0.62)	−0.39 (−1.19 to 0.40)	Resistance training	na	na	na
0.58 (−0.34 to 1.50)	−0.02 (−1.16 to 1.13)	0.38 (−0.63 to 1.39)	Mind−body exercise	na	na
0.55 (0.02 to 1.08)	−0.05 (−0.91 to 0.82)	0.35 (−0.33 to 1.02)	−0.03 (−1.10 to 1.03)	Aerobic exercise	na
0.44 (0.27 to 0.61)	−0.16 (−0.87 to 0.54)	0.23 (−0.21 to 0.68)	−0.15 (−1.08 to 0.79)	−0.11 (−0.67 to 0.45)	Combined exercise

B. Quality of life as measured by general questionnaires (after treatment)

Control	0.01 (−0.23 to 0.26)	0.13 (−0.01 to 0.27)	na	−0.05 (−0.25 to 0.15)	0.03 (−0.16 to 0.22)
0.01 (−0.36 to 0.37)	Walking	na	na	na	na
0.21 (0.00 to 0.42)	0.21 (−0.21 to 0.63)	Resistance training	na	−0.10 (−0.43 to 0.23)	na
na	na	na	Mind−body exercise	na	na
−0.07 (−0.53 to 0.39)	−0.08 (−0.66 to 0.51)	−0.29 (−0.78 to 0.21)	na	Aerobic exercise	na
−0.06 (−0.33 to 0.21)	−0.06 (−0.52 to 0.39)	−0.27 (−0.62 to 0.07)	na	0.01 (−0.52 to 0.55)	Combined exercise

C. Quality of life as measured by cancer-specific questionnaires (during treatment)

Control	0.35 (−0.03 to 0.72)	**0.15 (0.01 to 0.29)**	0.69 (−0.44 to 1.82)	**0.22 (0.05 to 0.40)**	**0.15 (0.03 to 0.27)**
0.43 (−0.11 to 0.96)	Walking	na	na	na	na
0.23 (−0.13 to 0.59)	−0.20 (−0.84 to 0.45)	Resistance training	na	0.06 (−0.30 to 0.42)	na
0.92 (0.34 to 1.51)	0.50 (−0.29 to 1.29)	**0.70 (0.01 to 1.38)**	Mind−body exercise	na	na
0.26 (−0.12 to 0.65)	−0.16 (−0.82 to 0.50)	0.03 (−0.44 to 0.50)	−0.66 (−1.36 to 0.04)	Aerobic exercise	0.05 (−0.57 to 0.67)
0.32 (0.03 to 0.61)	−0.10 (−0.71 to 0.51)	0.10 (−0.37 to 0.56)	−0.60 (−1.25 to 0.05)	0.06 (−0.41 to 0.53)	Combined exercise

D. Quality of life as measured by cancer-specific questionnaires (after treatment)

Control	**0.26 (0.03 to 0.49)**	0.25 (−0.06 to 0.55)	0.06 (−0.19 to 0.31)	0.05 (−0.15 to 0.24)	**0.28 (0.12 to 0.44)**
0.35 (0.01 to 0.68)	Walking	na	na	na	na
0.35 (−0.09 to 0.80)	0.01 (−0.55 to 0.56)	Resistance training	na	na	na
0.10 (−0.31 to 0.51)	−0.25 (−0.77 to 0.28)	−0.25 (−0.86 to 0.35)	Mind−body exercise	na	na
0.09 (−0.21 to 0.38)	−0.26 (−0.71 to 0.19)	−0.27 (−0.80 to 0.27)	0.02 (−0.49 to 0.52)	Aerobic exercise	na
0.41 (0.22 to 0.60)	0.06 (−0.32 to 0.45)	0.06 (−0.43 to 0.54)	0.31 (−0.14 to 0.76)	0.32 (−0.03 to 0.68)	Combined exercise

Notes: Data are effect sizes (95% confidence intervals). Effect sizes in bold are statistically significant. Positive effect sizes mean that the first intervention improves quality of life compared to the second intervention. Upper right triangle gives pooled effect sizes from pairwise comparisons (column intervention relative to row); lower left triangle gives pooled effect sizes from the network meta-analysis (row intervention relative to column).
Abbreviation: na = not available.

Table 3
League table of pooled effect sizes for physical and mental domains of quality of life.

A. Physical domain

Control	0.21 (−0.34 to 0.76)	0.13 (−0.26 to 0.52)	0.40 (−0.30 to 1.10)	0.12 (−0.38 to 0.61)	**0.56 (0.25** to **0.87)**
0.21 (−0.32 to 0.75)	Walking	na	na	na	na
0.12 (−0.24 to 0.47)	−0.10 (−0.74 to 0.55)	Resistance training	na	na	na
0.40 (−0.29 to 1.08)	0.18 (−0.69 to 1.05)	0.28 (−0.49 to 1.05)	Mind−body exercise	na	na
0.13 (−0.29 to 0.56)	−0.08 (−0.76 to 0.61)	0.02 (−0.48 to 0.51)	−0.26 (−1.07 to 0.54)	Aerobic exercise	na
0.52 (0.23 to 0.82)	0.31 (−0.30 to 0.92)	0.41 (−0.05 to 0.87)	0.13 (−0.62 to 0.87)	0.39 (−0.12 to 0.90)	Combined exercise

B. Mental domain

Control	0.21 (−0.40 to 0.82)	0.35 (−0.09 to 0.78)	0.40 (−0.37 to 1.17)	0.01 (−0.60 to 0.62)	**0.63 (0.26** to **1.00)**
0.21 (−0.39 to 0.82)	Walking	na	na	na	na
0.39 (−0.02 to 0.79)	0.18 (−0.55 to 0.91)	Resistance training	na	na	na
0.40 (−0.37 to 1.17)	0.19 (−0.79 to 1.17)	0.01 (−0.86 to 0.88)	Mind−body exercise	na	na
−0.07 (−0.60 to 0.46)	−0.28 (−1.08 to 0.53)	−0.46 (−1.05 to 0.14)	−0.47 (−1.41 to 0.46)	Aerobic exercise	na
0.59 (0.24 to 0.95)	0.38 (−0.32 to 1.08)	0.20 (−0.33 to 0.74)	0.19 (−0.65 to 1.04)	**0.66 (0.03 to 1.30)**	Combined exercise

Notes: Data are effect sizes (95% confidence intervals). Effect sizes in bold are statistically significant. Positive effect sizes mean that the first intervention improves quality of life compared to the second intervention. Upper right triangle gives the pooled effect sizes from pairwise comparisons (column intervention relative to row); lower left triangle gives pooled effect sizes from the network meta-analysis (row intervention relative to column).
Abbreviation: na = not available.

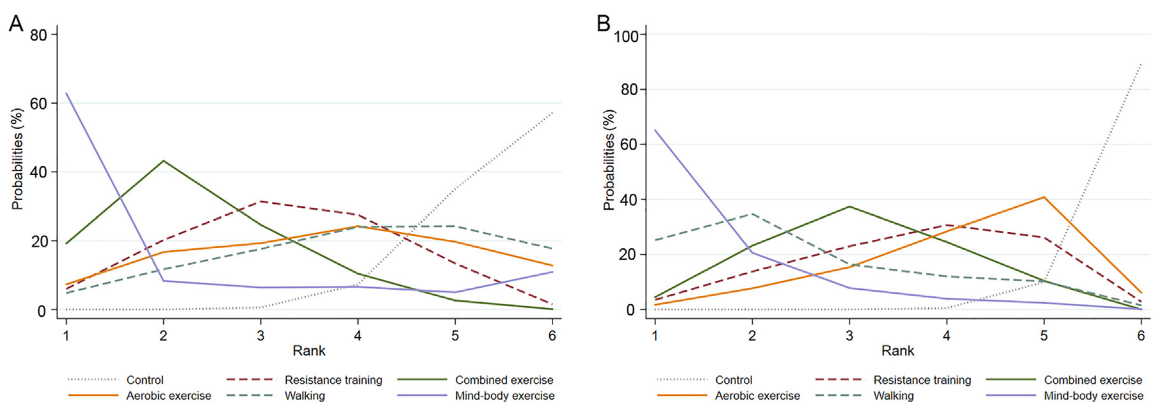

Fig. 3. Relative rankings for type of exercises on general and cancer-specific questionnaires of quality of life. (A) Quality of life measured by general questionnaires and (B) Quality of life as measured by cancer-specific questionnaires.

Comparisons with the control group for combined exercise and mind−body exercise showed considerable heterogeneity for HRQoL as measured by general and cancer-specific questionnaires ($I^2 = 87.8\%$, $\tau^2 = 0.198$; and $I^2 = 90.8\%$, $\tau^2 = 0.609$, respectively) (Supplementary Table 7).

3.4. Sensitivity analysis and publication bias

The pooled ES estimate was not significantly modified (by magnitude or direction) when individual study data were removed from the analysis one at a time.

Publication bias was found only for the comparison of the combined exercise *vs.* control group (Egger test $p = 0.067$) and aerobic exercise *vs.* control group (Egger test $p = 0.065$) for HRQoL as measured by cancer-specific questionnaire (Supplementary Fig. 5).

4. Discussion

In people with cancer, physical activity and exercise have a positive influence on physical fitness, fatigue, and physical and psychological well-being, all of which are components of the HRQoL construct. However, it is not entirely clear which exercise modality produces the best results.

Our systematic review and NMA, which included 93 RCTs involving nearly 7500 people with cancer, separated analyses by type of questionnaire used (general or cancer-specific), by timing of the exercise intervention (during or after treatment), and by physical and mental domains. The analyses showed that all types of exercise appear to have a positive effect on the HRQoL of people with cancer. None of the NMA estimates showed negative results; however, in most cases these estimates were not statistically significant, either due to the scarcity of studies and small sample sizes or because the ES was weak. In addition, our data suggest interventions combining aerobic activities with resistance training were the only exercise modality to result in a significant effect.

4.1. Exercise effects on HRQoL as measured by general and cancer-specific questionnaires

Both general and disease-specific questionnaires are widely used as outcome measures in clinical trials evaluating the effects of interventions in people with cancer, either during or after treatment. It is accepted that the use of cancer-specific questionnaires can be complemented by general questionnaires because while the formers are more sensitive to the psycho-emotional dimensions of HRQoL, generic scales, such as the Short Form 12 Health Survey, are more sensitive to the functional aspects of HRQoL.[121]

Our analyses independently examined the effects of exercise on HRQoL as measured by each of the questionnaire types. The NMA effect estimates (Table 2) showed that all exercise modalities had a positive effect on HRQoL when this construct was measured by general questionnaires, but that the effect was only significant for aerobic and combined exercise. When the outcome measure was a cancer-specific tool, all exercise modalities had a positive effect once again, but it was only significant for walking, mind−body exercise, and combined exercise.

The relative ranking (Fig. 3) shows aerobic and mind−body exercise to be the most effective exercise interventions when HRQoL was measured by general questionnaires, but it shows mind−body exercise and walking to be most effective when the outcome was measured by cancer-specific ones. However, these probabilities should be regarded with caution because both SUCRA values and *p* scores have important limitations. They are based only on relative effects against competing interventions, for example, and treatments that are poorly connected to the network of comparisons (e.g., mind−body exercise) often appear at the top of the ranking, even when these treatments are supported by less consistent or biased evidence.[122] Finally, some exercise modalities (aerobic and combined) are more frequently included in clinical trials in cancer patients likely because they are the same interventions recommended by influential scientific societies.[123]

4.2. Exercise during and after treatment

A decade ago, Mishra et al.[124] conducted a pair of pivotal systematic reviews looking at cancer patients during active treatment as well as at cancer survivors.[125] They concluded that exercise could benefit HRQoL and that supervised exercise was more effective than non-supervised exercise in this regard. However, they suggested more research was needed because of the heterogeneity of the exercise programs tested, the variety of HRQoL instruments used, and the risk of bias of the included trials. Following their lead, our own analyses distinguished between people undergoing active treatment for cancer and cancer survivors. Unfortunately, 10 years later, the evidence for the benefits of specific exercise modalities on HRQoL remains inconsistent.

Our network estimates suggest that during cancer treatment, combined exercise was the only modality to result in a significant effect on HRQoL as measured by general questionnaires; when HRQoL was measured by cancer-specific questionnaires, both mind−body and combined exercise showed significant effects. However, after cancer treatment, combined exercise and walking were the only exercise modalities to suggest significant effects, and only when HRQoL was measured by cancer-specific questionnaires. These results are partially in line with those reported by Gerritsen and Vincent[126] which suggested that exercise leads to benefits in a variety of socio-emotional areas, including improvements in physical and mental domains, but only during cancer treatment; our data additionally suggest benefits from walking and combined exercise after cancer treatment. Moreover, our data confirm those reported in a systematic review and meta-analysis by Ramírez-Vélez et al.[127] showing that combined exercise at moderate-to-vigorous intensity has significantly improved HRQoL levels in women with breast cancer; but our data also suggest that cancer patients may elicit benefits to their HRQoL from most modalities of exercise. Our findings are in line with data from a review of 69 guidelines developed under the auspices of the World Health Organization,[128] which include low intensity exercise, such as walking or mind−body exercises, as effective strategies that result in benefits to the physical and psychological domains of HRQoL.

The scarcity (or even absence, in some modalities) of studies examining the effects of exercise on the HRQoL of cancer survivors makes us very cautious about interpreting our results. Perhaps the only solid conclusion we can draw from these analyses is that, as Mishra et al.[125] recommended a decade ago, well-designed research initiatives with sufficient sample sizes are strongly needed to progress research on the effects of exercise on the HRQoL of people with cancer, especially over the long term.

4.3. Exercise effects on physical and mental domains

HRQoL is a multidimensional construct that is generally agreed to include physical well-being along with social and psychological functioning. However, given that social functioning is strongly determined by socio-economic variables related to family and social determinants that are more difficult to influence (e.g., socio-economic status or access to care), it is very common for many HRQoL assessment scales to synthesize their scores into two domains: physical and mental well-being; but it must be recognized that each of these has a two-way relationship with social functioning. Therefore, to provide an overview of potential differences in the effects of exercise on the physical and mental dimensions of HRQoL, we conducted separate analyses for these 2 domains.

As with previous analyses, our NMA pooled estimates suggest that all exercise modalities have a beneficial effect on the physical and mental domains of HRQoL, but this effect was only significant for combined exercise. Furthermore, our results suggest that the magnitude of the effect is very similar in both domains. These results are not surprising if we consider that physical health is closely related to mental health, and that both are influenced by socio-economic determinants.[129]

4.4. Limitations

Our systematic review and NMA have some limitations to be acknowledged. The primary limitation of this NMA is related to the scarcity of studies, the disparity of their designs, and their lack of statistical power. However, based on the existing research, it would be redundant to conduct a multiple-exercise intervention meta-analysis without making any effort to present comparisons between the different types of exercise. For this reason, we comprehensively synthesized the existing data into an NMA to present indirect pooled estimates. We have pointed repeatedly above to the limitations of this methodology when direct treatment comparison studies are scarce.[122] Second, and closely related, although we present ranking probabilities of treatments as estimates of the average certainty that one treatment is better than another for a given outcome, we are conscious of the limitations of these approaches to ranking treatments (e.g., they are based only on the relative effect and disregard that treatments with scarcity of comparisons tend to rank higher in spite of the weakness of the evidence in favor of such treatments[130]). Third, exercise interventions cannot be blinded; thus, intervention-group patients may be prone to the Hawthorne effect[131] (e.g., patients in an exercise group may behave in what they perceive to be an improved way because they know their outcomes are being compared to those of a control group). Furthermore, in studies comparing 2 types of exercise, it is not possible to know whether patients dropped out of follow-up because the randomization process did not assign them to the type of exercise they preferred. Fourth, most studies did not control for the type or stage of cancer, the treatment that patients underwent, or for the patient's lifestyle before and after the diagnosis, all of which are characteristics of cancer and treatment that influence HRQoL levels. Fifth, studies did not present results adjusting for HRQoL levels at baseline; thus, floor and ceiling effects[132] could bias estimates such that people who have poorer HRQoL levels at baseline have more room for increase than those with high baseline HRQoL levels. Finally, there were great heterogeneities in the frequency, intensity, duration, and supervision of interventions, suggesting the need to further the reproducibility of interventions by better describing their characteristics and justifying why the relevant exercise modality is being tested in each clinical trial.

5. Conclusion

Our systematic review and NMA suggest that all exercise modalities may exert a positive effect on HRQoL, as none of the NMA estimates showed negative results. Our estimates suggested that programs combining aerobic and resistance training were the only ones to result in a statistically significant positive effect on HRQoL levels as measured by both general and cancer-specific tools. Furthermore, our data show that combined exercise is the only exercise modality to show a significant effect on patients during treatment regardless of the type of questionnaire with which HRQoL is assessed. Last, our NMA estimates also suggest that combined exercise is the only modality effective at improving both the physical and mental domains of HRQoL. Therefore, in line with international consensus and guidelines, exercise should be recommended for improving HRQoL in patients with cancer, but only with the understanding that the evidence behind this recommendation is weak. In summary, based on the available evidence, exercise programs combining aerobic and resistance training can be recommended as an adjunct to disease therapy in people with cancer during and following medical intervention. Furthermore, we encourage the launch of well-designed RCTs to determine what kinds of exercise are most advisable depending on tumor type, stage of progression, and other personal characteristics of patients, including age and type of treatment.

Data availability

After the publication of this article, the full dataset will be available in online Mendeley Data, a repository of research data that allows the assignment of a permanent digital object identifier, in such a way that the data of this study can be easily referenced (doi: 10.17632/2c4y6k32g5.1).

Acknowledgments

This work was supported by the European Regional Development Fund. Supported by Consejería de Educación, Cultura y Deportes-JCCM, and Fondo Europeo de Desarrollo Regional funds (grant no. SBPLY/17/180501/000533). SRG is supported by a grant from the University of Castilla-La Mancha (2020-PREDUCLM-15596). BBP is supported by a grant from the Universidad de Castilla-La Mancha co-financed by the European Social Fund (2020-PREDUCLM-16746).

Authors' contributions

VMV (Principal investigator), ICR, and EUG were the core team leading this systematic review and NMA; SRG, LGM, JJGC, BBP, and FRA have made substantial contributions to acquisition, analysis and interpretation of data, drafting the article, or revising it critically for important intellectual content. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests.

Supplementary materials

Supplementary materials associated with this article can be found in the online version at doi:10.1016/j.jshs.2023.01.002.

References

1. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;**71**:209–49.
2. Costa AR, Alves L, Lunet N. Healthcare services and medication use among cancer survivors and their partners: A cross-sectional analysis of 16 European countries. *J Cancer Surviv* 2020;**14**:720–30.
3. Roila F, Cortesi E. Quality of life as a primary end point in oncology. *Ann Oncol* 2001;**12**(Suppl. 3):S3–6.
4. Shrestha A, Martin C, Burton M, Walters S, Collins K, Wyld L. Quality of life versus length of life considerations in cancer patients: A systematic literature review. *Psychooncology* 2019;**28**:1367–80.
5. Gilchrist SC, Barac A, Ades PA, et al. Cardio-oncology rehabilitation to manage cardiovascular outcomes in cancer patients and survivors: A scientific statement from the American Heart Association. *Circulation* 2019;**139**:e997–1012.
6. Zhang QB, Zhang BH, Zhang KZ, et al. Moderate swimming suppressed the growth and metastasis of the transplanted liver cancer in mice model: With reference to nervous system. *Oncogene* 2016;**35**:4122–31.
7. Pedersen L, Idorn M, Olofsson GH, et al. Voluntary running suppresses tumor growth through epinephrine- and IL-6-dependent NK cell mobilization and redistribution. *Cell Metab* 2016;**23**:554–62.
8. Fiuza-Luces C, Garatachea N, Berger NA, Lucia A. Exercise is the real polypill. *Physiology (Bethesda)* 2013;**28**:330–58.
9. Scott JM, Zabor EC, Schwitzer E, et al. Efficacy of exercise therapy on cardiorespiratory fitness in patients with cancer: A systematic review and meta-analysis. *J Clin Oncol* 2018;**36**:2297–305.
10. Schneider CM, Hsieh CC, Sprod LK, Carter SD, Hayward R. Cancer treatment-induced alterations in muscular fitness and quality of life: The role of exercise training. *Ann Oncol* 2007;**18**:1957–62.
11. Sweegers MG, Altenburg TM, Chinapaw MJ, et al. Which exercise prescriptions improve quality of life and physical function in patients with cancer during and following treatment? A systematic review and meta-analysis of randomised controlled trials. *Br J Sports Med* 2018;**52**:505–13.
12. Stout NL, Baima J, Swisher A, Winters-Stone KM, Welsh J. A systematic review of exercise systematic reviews in the cancer literature (2005−2017). *PM R* 2017;**9**(Suppl. 2):S347–84.
13. Campbell KL, Winters-Stone KM, Wiskemann J, et al. Exercise guidelines for cancer survivors: Consensus statement from international multidisciplinary roundtable. *Med Sci Sports Exerc* 2019;**51**:2375–90.
14. Hutton B, Catalá-López F, Moher D. The PRISMA statement extension for systematic reviews incorporating network meta-analysis: PRISMA-NMA. *Med Clin (Barc)* 2016;**147**:262–6.
15. Higgins J, Thomas J, Chandler J, et al. *Cochrane handbook for systematic reviews of interventions*. *Version 2.0 (updated July 2019)*. Available at: www.training.cochrane.org/handbook. [accessed 10.10.2022].
16. Ubago-Guisado E, Gracia-Marco L, Cavero-Redondo I, et al. Effect of different types of exercise on health-related quality of life during and after cancer treatment: A protocol for a systematic review and network meta-analysis. *BMJ Open* 2019;**9**: e031374. doi:10.1136/bmjopen-2019-031374.
17. McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. *J Clin Epidemiol* 2016;**75**:40–6.
18. Deeks J, Higgins J, Altman D. Analysing data and undertaking meta-analyses. editors. In: Higgins J, Thomas J, editors. *Cochrane handbook for systematic reviews of interventions*. Chichester, West Sussex: Willey Blackwell; 2019.p.241–84.
19. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: Definitions and distinctions for health-related research. *Public Health Rep* 1985;**100**:126–31.
20. Sterne J, Savović J, Page M, et al. RoB 2: A revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898. doi:10.1136/bmj.l4898.
21. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction−GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;**64**:383–94.
22. Salanti G, Ades AE, Ioannidis JPA. Graphical methods and numerical summaries for presenting results from multiple-treatment meta-analysis: An overview and tutorial. *J Clin Epidemiol* 2011;**64**:163–71.
23. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;**7**:177–88.
24. Stettler C, Allemann S, Wandel S, et al. Drug eluting and bare metal stents in people with and without diabetes: Collaborative network meta-analysis. *BMJ* 2008;**337**:668–72.
25. Chaimani A, Higgins JPT, Mavridis D, Spyridonos P, Salanti G. Graphical tools for network meta-analysis in STATA. *PLoS One* 2013;**8**: e76654. doi:10.1371/journal.pone.0076654.
26. Rücker G, Schwarzer G. Ranking treatments in frequentist network meta-analysis works without resampling methods. *BMC Med Res Methodol* 2015;**15**:58. doi:10.1186/s12874-015-0060-8.
27. Sterne JAC, Egger M, Smith GD. Investigating and dealing with publication and other biases in meta-analysis. *BMJ* 2001;**323**:101–5.
28. Adamsen L, Quist M, Andersen C, et al. Effect of a multimodal high intensity exercise intervention in cancer patients undergoing chemotherapy: Randomised controlled trial. *BMJ* 2009;**339**:b3410. doi:10.1136/bmj.b3410.
29. Allen SK, Brown V, White D, et al. Multimodal prehabilitation during neoadjuvant therapy prior to esophagogastric cancer resection: Effect on cardiopulmonary exercise test performance, muscle mass and quality of life—A pilot randomized clinical trial. *Ann Surg Oncol* 2022;**29**:1839–50.
30. Andersen C, Rørth M, Ejlertsen B, et al. The effects of a six-week supervised multimodal exercise intervention during chemotherapy on cancer-related fatigue. *Eur J Oncol Nurs* 2013;**17**:331–9.
31. Arbane G, Tropman D, Jackson D, Garrod R. Evaluation of an early exercise intervention after thoracotomy for non-small cell lung cancer (NSCLC), effects on quality of life, muscle strength and exercise tolerance: Randomised controlled trial. *Lung Cancer* 2011;**71**:229–34.
32. Backman M, Wengström Y, Johansson B, et al. A randomized pilot study with daily walking during adjuvant chemotherapy for patients with breast and colorectal cancer. *Acta Oncol* 2014;**53**:510–20.
33. Baumann FT, Kraut L, Schüle K, Bloch W, Fauser AA. A controlled randomized study examining the effects of exercise therapy on patients undergoing haematopoietic stem cell transplantation. *Bone Marrow Transplant* 2010;**45**:355–62.
34. Baumann FT, Zopf EM, Nykamp E, et al. Physical activity for patients undergoing an allogeneic hematopoietic stem cell transplantation: Benefits of a moderate exercise intervention. *Eur J Haematol* 2011;**87**:148–56.
35. Bourke L, Doll H, Crank H, Daley A, Rosario D, Saxton JM. Lifestyle intervention in men with advanced prostate cancer receiving androgen suppression therapy: A feasibility study. *Cancer Epidemiol Biomarkers Prev* 2011;**20**:647–57.
36. Broderick JM, Guinan E, Kennedy MJ, et al. Feasibility and efficacy of a supervised exercise intervention in de-conditioned cancer survivors during the early survivorship phase: The PEACH trial. *J Cancer Surviv* 2013;**7**:551–62.
37. Brown JC, Sarwer DB, Troxel AB, et al. A randomized trial of exercise and diet on health-related quality of life in survivors of breast cancer with overweight or obesity. *Cancer* 2021;**127**:3856–64.
38. Buffart LM, Ros WJ, Chinapaw MJ, et al. Mediators of physical exercise for improvement in cancer survivors' quality of life. *Psychooncology* 2014;**23**:330–8.
39. Buffart LM, Newton RU, Chinapaw MJ, et al. The effect, moderators, and mediators of resistance and aerobic exercise on health-related quality of life in older long-term survivors of prostate cancer. *Cancer* 2015;**121**:2821–30.
40. Buffart LM, Galvao DA, Chinapaw MJ, et al. Mediators of the resistance and aerobic exercise intervention effect on physical and general health in men undergoing androgen deprivation therapy for prostate cancer. *Cancer* 2014;**120**:294–301.
41. Cadmus LA, Salovey P, Yu H, Chung G, Kasl S, Irwin ML. Exercise and quality of life during and after treatment for breast cancer: Results of two randomized controlled trials. *Psychooncology* 2009;**18**:343–52.
42. Casla S, López-Tarruella S, Jerez Y, et al. Supervised physical exercise improves VO_{2max}, quality of life, and health in early stage breast cancer

patients: A randomized controlled trial. *Breast Cancer Res Treat* 2015;**153**:371–82.
43. Chandwani KD, Perkins G, Nagendra HR, et al. Randomized, controlled trial of yoga in women with breast cancer undergoing radiotherapy. *J Clin Oncol* 2014;**32**:1058–65.
44. Chen Z, Meng Z, Milbury K, et al. Qigong improves quality of life in women undergoing radiotherapy for breast cancer: Results of a randomized controlled trial. *Cancer* 2013;**119**:1690–8.
45. Chuang TY, Yeh ML, Chung YC. A nurse facilitated mind-body interactive exercise (Chan-Chuang qigong) improves the health status of non-Hodgkin lymphoma patients receiving chemotherapy: Randomised controlled trial. *Int J Nurs Stud* 2017;**69**:25–33.
46. Cormie P, Galvao DA, Spry N, et al. Can supervised exercise prevent treatment toxicity in patients with prostate cancer initiating androgen-deprivation therapy: A randomised controlled trial. *BJU Int* 2015;**115**:256–66.
47. Cormie P, Newton RU, Spry N, Joseph D, Taaffe DR, Galvao DA. Safety and efficacy of resistance exercise in prostate cancer patients with bone metastases. *Prostate Cancer Prostatic Dis* 2013;**16**:328–35.
48. Cormie P, Pumpa K, Galvão DA, et al. Is it safe and efficacious for women with lymphedema secondary to breast cancer to lift heavy weights during exercise: A randomised controlled trial. *J Cancer Surviv* 2013;**7**:413–24.
49. Courneya KS, Friedenreich CM, Quinney HA, Fields AL, Jones LW, Fairey AS. A randomized trial of exercise and quality of life in colorectal cancer survivors. *Eur J Cancer Care* 2003;**12**:347–57.
50. Courneya KS, Mackey JR, Bell GJ, Jones LW, Field CJ, Fairey AS. Randomized controlled trial of exercise training in postmenopausal breast cancer survivors: Cardiopulmonary and quality of life outcomes. *J Clin Oncol* 2003;**21**:1660–8.
51. Culos-Reed SN, Carlson LE, Daroux LM, Hately-Aldous S. A pilot study of yoga for breast cancer survivors: physical and psychological benefits. *Psychooncology* 2006;**15**:891–7.
52. Culos-Reed SN, Robinson JW, Lau H, et al. Physical activity for men receiving androgen deprivation therapy for prostate cancer: Benefits from a 16-week intervention. *Support Care Cancer* 2010;**18**:591–9.
53. Danhauer SC, Mihalko SL, Russell GB, et al. Restorative yoga for women with breast cancer: Findings from a randomized pilot study. *Psychooncology* 2009;**18**:360–8.
54. De Luca V, Minganti C, Borrione P, et al. Effects of concurrent aerobic and strength training on breast cancer survivors: A pilot study. *Public Health* 2016;**136**:126–32.
55. Dimeo FC, Thomas F, Raabe-Menssen C, Pröpper F, Mathias M. Effect of aerobic exercise and relaxation training on fatigue and physical performance of cancer patients after surgery. A randomised controlled trial. *Support Care Cancer* 2004;**12**:774–9.
56. Donnelly CM, Blaney JM, Lowe-Strong A, et al. A randomised controlled trial testing the feasibility and efficacy of a physical activity behavioural change intervention in managing fatigue with gynaecological cancer survivors. *Gynecol Oncol* 2011;**122**:618–24.
57. Dronkers JJ, Lamberts H, Reutelingsperger IM, et al. Preoperative therapeutic programme for elderly patients scheduled for elective abdominal oncological surgery: A randomized controlled pilot study. *Clin Rehabil* 2010;**24**:614–22.
58. Dunne DF, Jack S, Jones RP, et al. Randomized clinical trial of prehabilitation before planned liver resection. *Br J Surg* 2016;**103**:504–12.
59. Edvardsen E, Skjønsberg OH, Holme I, Nordsletten L, Borchsenius F, Anderssen SA. High-intensity training following lung cancer surgery: A randomised controlled trial. *Thorax* 2015;**70**:244–50.
60. Ergun M, Eyigor S, Karaca B, Kisim A, Uslu R. Effects of exercise on angiogenesis and apoptosis-related molecules, quality of life, fatigue and depression in breast cancer patients. *Eur J Cancer Care* 2013;**22**:626–37.
61. Eyigor S, Karapolat H, Yesil H, Uslu R, Durmaz B. Effects of Pilates exercises on functional capacity, flexibility, fatigue, depression and quality of life in female breast cancer patients: A randomized controlled study. *Eur J Phys Rehabil Med* 2010;**46**:481–7.
62. Fillion L, Gagnon P, Leblond F, et al. A brief intervention for fatigue management in breast cancer survivors. *Cancer Nurs* 2008;**31**:145–59.
63. Furzer BJ, Ackland TR, Wallman KE, et al. A randomised controlled trial comparing the effects of a 12-week supervised exercise versus usual care on outcomes in haematological cancer patients. *Support Care Cancer* 2016;**24**:1697–707.
64. Galiano-Castillo N, Cantarero-Villanueva I, Fernández-Lao C, et al. Telehealth system: A randomized controlled trial evaluating the impact of an internet-based exercise intervention on quality of life, pain, muscle strength, and fatigue in breast cancer survivors. *Cancer* 2016;**122**:3166–74.
65. Galvao DA, Spry N, Denham J, et al. A multicentre year-long randomised controlled trial of exercise training targeting physical functioning in men with prostate cancer previously treated with androgen suppression and radiation from TROG 03.04 RADAR. *Eur Urol* 2014;**65**:856–64.
66. García-Soidán JL, Pérez-Ribao I, Leirós-Rodríguez R, Soto-Rodríguez A. Long-term influence of the practice of physical activity on the self-perceived quality of life of women with breast cancer: A randomized controlled trial. *Int J Environ Res Public Health* 2020;**17**:4986. doi:10.3390/ijerph17144986.
67. Granger CL, Chao C, McDonald CF, Berney S, Denehy L. Safety and feasibility of an exercise intervention for patients following lung resection: A pilot randomized controlled trial. *Integr Cancer Ther* 2012;**12**:213–24.
68. Hacker ED, Larson J, Kujath A, Peace D, Rondelli D, Gaston L. Strength training following hematopoietic stem cell transplantation. *Cancer Nurs* 2011;**34**:238–49.
69. Hagstrom AD, Marshall PW, Lonsdale C, Cheema BS, Fiatarone Singh MA, Green S. Resistance training improves fatigue and quality of life in previously sedentary breast cancer survivors: A randomised controlled trial. *Eur J Cancer Care (Engl)* 2016;**25**:784–94.
70. Haines TP, Sinnamon P, Wetzig NG, et al. Multimodal exercise improves quality of life of women being treated for breast cancer, but at what cost? Randomized trial with economic evaluation. *Breast Cancer Res Treat* 2010;**124**:163–75.
71. Hayes S, Davies PS, Parker T, Bashford J, Newman B. Quality of life changes following peripheral blood stem cell transplantation and participation in a mixed-type, moderate-intensity, exercise program. *Bone Marrow Transplant* 2004;**33**:553–8.
72. Henke CC, Cabri J, Fricke L, et al. Strength and endurance training in the treatment of lung cancer patients in stages IIIA/IIIB/IV. *Support Care Cancer* 2014;**22**:95–101.
73. Ho M, Ho JWC, Fong DYT, et al. Effects of dietary and physical activity interventions on generic and cancer-specific health-related quality of life, anxiety, and depression in colorectal cancer survivors: A randomized controlled trial. *J Cancer Surviv* 2020;**14**:424–33.
74. Hojan K, Kwiatkowska-Borowczyk E, Leporowska E, et al. Physical exercise for functional capacity, blood immune function, fatigue, and quality of life in high-risk prostate cancer patients during radiotherapy: A prospective, randomized clinical study. *Eur J Phys Rehabil Med* 2016;**52**:489–501.
75. Hojan K, Kwiatkowska-Borowczyk E, Leporowska E, Milecki P. Inflammation, cardiometabolic markers, and functional changes in men with prostate cancer. A randomized controlled trial of a 12 month exercise program. *Pol Arch Intern Med* 2017;**127**:25–35.
76. Hornsby WE, Douglas PS, West MJ, et al. Safety and efficacy of aerobic training in operable breast cancer patients receiving neoadjuvant chemotherapy: A phase II randomized trial. *Acta Oncol* 2014;**53**:65–74.
77. Hwang CL, Yu CJ, Shih JY, Yang PC, Wu YT. Effects of exercise training on exercise capacity in patients with non-small cell lung cancer receiving targeted therapy. *Support Care Cancer* 2012;**20**:3169–77.
78. Hwang JH, Chang HJ, Shim YH, et al. Effects of supervised exercise therapy in patients receiving radiotherapy for breast cancer. *Yonsei Med J* 2008;**49**:443–50.
79. Jarden M, Baadsgaard MT, Hovgaard DJ, Boesen E, Adamsen L. A randomized trial on the effect of a multimodal intervention on physical capacity, functional performance and quality of life in adult patients undergoing allogeneic SCT. *Bone Marrow Transplant* 2009;**43**:725–37.
80. Kang DW, Fairey AS, Boulé NG, Field CJ, Wharton SA, Courneya KS. A randomized trial of the effects of exercise on anxiety, fear of cancer

progression and quality of life in prostate cancer patients on active surveillance. *J Urol* 2022;**207**:814–22.
81. Kampshoff CS, Chinapaw MJ, Brug J, et al. Randomized controlled trial of the effects of high intensity and low-to-moderate intensity exercise on physical fitness and fatigue in cancer survivors: Results of the Resistance and Endurance exercise After ChemoTherapy (REACT) study. *BMC Med* 2015;**13**:275. doi:10.1186/s12916-015-0513-2.
82. Knols RH, de Bruin ED, Uebelhart D, et al. Effects of an outpatient physical exercise program on hematopoietic stem-cell transplantation recipients: A randomized clinical trial. *Bone Marrow Transplant* 2011;**46**:1245–55.
83. Lai Y, Huang J, Yang M, Su J, Liu J, Che G. Seven-day intensive preoperative rehabilitation for elderly patients with lung cancer: A randomized controlled trial. *J Surg Res* 2017;**209**:30–6.
84. Lee EO, Chae YR, Song R, Eom A, Lam P, Heitkemper M. Feasibility and effects of a tai chi self-help education program for Korean gastric cancer survivors. *Oncol Nurs Forum* 2010;**37**:E1–6.
85. Littman AJ, Bertram LC, Ceballos R, et al. Randomized controlled pilot trial of yoga in overweight and obese breast cancer survivors: Effects on quality of life and anthropometric measures. *Support Care Cancer* 2012;**20**:267–77.
86. Livingston PM, Craike MJ, Salmon J, et al. Effects of a clinician referral and exercise program for men who have completed active treatment for prostate cancer: A multicenter cluster randomized controlled trial (ENGAGE). *Cancer* 2015;**121**:2646–54.
87. Lotzke D, Wiedemann F, Rodrigues Recchia D, et al. Iyengar-yoga compared to exercise as a therapeutic intervention during (neo)adjuvant therapy in women with Stage I−III breast cancer: Health-related quality of life, mindfulness, spirituality, life satisfaction, and cancer-related fatigue. *Evid Based Complement Altern Med* 2016;**2016**:5931816. doi:10.1155/2016/5931816.
88. Mardani A, Pedram Razi S, Mazaheri R, Haghani S, Vaismoradi M. Effect of the exercise programme on the quality of life of prostate cancer survivors: A randomized controlled trial. *Int J Nurs Pract* 2021;**27**: e12883. doi:10.1111/ijn.12883.
89. McNeely ML, Parliament M, Courneya KS, et al. A pilot study of a randomized controlled trial to evaluate the effects of progressive resistance exercise training on shoulder dysfunction caused by spinal accessory neurapraxia/neurectomy in head and neck cancer survivors. *Head Neck* 2004;**26**:518–30.
90. McNeely ML, Parliament MB, Seikaly H, et al. Effect of exercise on upper extremity pain and dysfunction in head and neck cancer survivors: A randomized controlled trial. *Cancer* 2008;**113**:214–22.
91. Mijwel S, Backman M, Bolam KA, et al. Adding high-intensity interval training to conventional training modalities: Optimizing health-related outcomes during chemotherapy for breast cancer: The OptiTrain randomized controlled trial. *Breast Cancer Res Treat* 2018;**168**:79–93.
92. Moonsammy SH, Guglietti CL, Santa Mina D, et al. A pilot study of an exercise & cognitive behavioral therapy intervention for epithelial ovarian cancer patients. *J Ovarian Res* 2013;**6**:21. doi:10.1186/1757-2215-6-21.
93. Moraes RF, Ferreira-Júnior JB, Marques VA, et al. Resistance training, fatigue, quality of life, anxiety in breast cancer survivors. *J strength Cond Res* 2021;**35**:1350–6.
94. Morano MT, Mesquita R, Da Silva GP, et al. Comparison of the effects of pulmonary rehabilitation with chest physical therapy on the levels of fibrinogen and albumin in patients with lung cancer awaiting lung resection: A randomized clinical trial. *BMC Pulm Med* 2014;**14**:121. doi:10.1186/1471-2466-14-121.
95. Morielli AR, Boulé NG, Usmani N, et al. Effects of exercise during and after neoadjuvant chemoradiation on symptom burden and quality of life in rectal cancer patients: A phase II randomized controlled trial. *J Cancer Surviv* 2021. doi:10.1007/s11764-021-01149-w.
96. Mutrie N, Campbell A, Barry S, et al. Five-year follow-up of participants in a randomised controlled trial showing benefits from exercise for breast cancer survivors during adjuvant treatment. Are there lasting effects? *J Cancer Surviv* 2012;**6**:420–30.
97. Mutrie N, Campbell AM, Whyte F, et al. Benefits of supervised group exercise programme for women being treated for early stage breast cancer: Pragmatic randomised controlled trial. *BMJ* 2007;**334**:517. doi:10.1136/bmj.39094.648553.AE.
98. Nilsen TS, Raastad T, Skovlund E, et al. Effects of strength training on body composition, physical functioning, and quality of life in prostate cancer patients during androgen deprivation therapy. *Acta Oncol* 2015;**54**:1805–13.
99. Persoon S, ChinApaw MJM, Buffart LM, et al. Randomized controlled trial on the effects of a supervised high intensity exercise program in patients with a hematologic malignancy treated with autologous stem cell transplantation: Results from the EXIST study. *PLoS One* 2017;**12**: e0181313. doi:10.1371/journal.pone.0181313.
100. Pinto B, Stein K, Dunsiger S. Peer mentorship to promote physical activity among cancer survivors: Effects on quality of life. *Psychooncology* 2015;**24**:1295–302.
101. Reis D, Walsh ME, Young-McCaughan S, Jones T. Effects of Nia exercise in women receiving radiation therapy for breast cancer. *Oncol Nurs Forum* 2013;**40**:E374–81.
102. Rogers LQ, Anton PM, Fogleman A, et al. Pilot, randomized trial of resistance exercise during radiation therapy for head and neck cancer. *Head Neck* 2013;**35**:1178–88.
103. Rogers LQ, Courneya KS, Anton PM, et al. Effects of the BEAT Cancer physical activity behavior change intervention on physical activity, aerobic fitness, and quality of life in breast cancer survivors: A multicenter randomized controlled trial. *Breast Cancer Res Treat* 2015;**149**:109–19.
104. Rogers LQ, Hopkins-Price P, Vicari S, et al. A randomized trial to increase physical activity in breast cancer survivors. *Med Sci Sport Exerc* 2009;**41**:935–46.
105. Rutkowska A, Rutkowski S, Wrzeciono A, Czech O, Szczegielniak J, Jastrzębski D. Short-term changes in quality of life in patients with advanced lung cancer during in-hospital exercise training and chemotherapy treatment: A randomized controlled trial. *J Clin Med* 2021;**10**:1761. doi:10.3390/jcm10081761.
106. Samuel SR, Maiya GA, Babu AS, Vidyasagar MS. Effect of exercise training on functional capacity & quality of life in head & neck cancer patients receiving chemoradiotherapy. *Indian J Med Res* 2013;**137**:515–20.
107. Sandel SL, Judge JO, Landry N, Faria L, Ouellette R, Majczak M. Dance and movement program improves quality-of-life measures in breast cancer survivors. *Cancer Nurs* 2005;**28**:301–9.
108. Schmidt T, Weisser B, Durkop J, et al. Comparing endurance and resistance training with standard care during chemotherapy for patients with primary breast cancer. *Anticancer Res* 2015;**35**:5623–9.
109. Schmidt ME, Wiskemann J, Armbrust P, Schneeweiss A, Ulrich CM, Steindorf K. Effects of resistance exercise on fatigue and quality of life in breast cancer patients undergoing adjuvant chemotherapy: A randomized controlled trial. *Int J Cancer* 2015;**137**:471–80.
110. Segal RJ, Reid RD, Courneya KS, et al. Randomized controlled trial of resistance or aerobic exercise in men receiving radiation therapy for prostate cancer. *J Clin Oncol* 2009;**27**:344–51.
111. Siedentopf F, Utz-Billing I, Gairing S, Schoenegg W, Kentenich H, Kollak I. Yoga for patients with early breast cancer and its impact on quality of life−A randomized controlled trial. *Geburtshilfe Frauenheilkd* 2013;**73**:311–7.
112. Spahn G, Choi KE, Kennemann C, et al. Can a multimodal mind-body program enhance the treatment effects of physical activity in breast cancer survivors with chronic tumor-associated fatigue? A randomized controlled trial. *Integr Cancer Ther* 2013;**12**:291–300.
113. Speck RM, Gross CR, Hormes JM, et al. Changes in the body image and relationship scale following a one-year strength training trial for breast cancer survivors with or at risk for lymphedema. *Breast Cancer Res Treat* 2010;**121**:421–30.
114. Steindorf K, Schmidt ME, Klassen O, et al. Randomized, controlled trial of resistance training in breast cancer patients receiving adjuvant radiotherapy: Results on cancer-related fatigue and quality of life. *Ann Oncol* 2014;**25**:2237–43.
115. Tang MF, Liou TH, Lin CC. Improving sleep quality for cancer patients: Benefits of a home-based exercise intervention. *Support Care Cancer* 2010;**18**:1329–39.

116. Wang YJ, Boehmke M, Wu YW, Dickerson SS, Fisher N. Effects of a 6-week walking program on “Taiwanese” women newly diagnosed with early-stage breast cancer. *Cancer Nurs* 2011;**34**:E1–13.
117. Winters-Stone KM, Lyons KS, Dobek J, et al. Benefits of partnered strength training for prostate cancer survivors and spouses: Results from a randomized controlled trial of the Exercising Together project. *J Cancer Surviv* 2016;**10**:633–44.
118. Wiskemann J, Dreger P, Schwerdtfeger R, et al. Effects of a partly self-administered exercise program before, during, and after allogeneic stem cell transplantation. *Blood* 2011;**117**:2604–13.
119. Yagli N V, Ulger O. The effects of yoga on the quality of life and depression in elderly breast cancer patients. *Complement Ther Clin Pract* 2015;**21**:7–10.
120. Zopf EM, Bloch W, Machtens S, et al. Effects of a 15-month supervised exercise program on physical and psychological outcomes in prostate cancer patients following prostatectomy: The ProRehab Study. *Integr Cancer Ther* 2015;**14**:409–18.
121. Schipper H, Clinch J, Powell V. Definitions and conceptual issues. In: Spilker B, editor. *Quality of life assessments in clinical trials*. New York, NY: Lippincott Williams and Wilkins; 1990.p.11–24.
122. Mbuagbaw L, Rochwerg B, Jaeschke R, et al. Approaches to interpreting and choosing the best treatments in network meta-analyses. *Syst Rev* 2017;**6**:79. doi:10.1186/s13643-017-0473-z.
123. Cancer.Net. *Editorial Board. Exercise During Cancer Treatment*. Available at: https://www.cancer.net/survivorship/healthy-living/exercise-during-cancer-treatment. [accessed 10.08.2022].
124. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. *Cochrane Database Syst Rev 2012*; 2012:CD008465. doi:10.1002/14651858.CD008465.pub2.
125. Mishra SI, Scherer RW, Geigle PM, et al. Exercise interventions on health-related quality of life for cancer survivors. *Cochrane Database Syst Rev* 2012;**2012**:007566. doi:10.1002/14651858.CD007566.pub2.
126. Gerritsen JKW, Vincent AJPE. Exercise improves quality of life in patients with cancer: A systematic review and meta-analysis of randomised controlled trials. *Br J Sports Med* 2016;**50**:796–803.
127. Ramírez-Vélez R, Zambom-Ferraresi F, García-Hermoso A, Kievisiene J, Rauckiene-Michealsson A, Agostinis-Sobrinho C. Evidence-based exercise recommendations to improve mental wellbeing in women with breast cancer during active treatment: A systematic review and meta-analysis. *Cancers (Basel)* 2021;**13**:1–28.
128. Stout NL, Santa Mina D, Lyons KD, Robb K, Silver JK. A systematic review of rehabilitation and exercise recommendations in oncology guidelines. *CA Cancer J Clin* 2021;**71**:149–75.
129. Naughton MJ, Weaver KE. Physical and mental health among cancer survivors: Considerations for long-term care and quality of life. *N C Med J* 2014;**75**:283–6.
130. Chaimani A, Porcher R, Sbidian É, Mavridis D. A Markov chain approach for ranking treatments in network meta-analysis. *Stat Med* 2021;**40**:451–64.
131. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. *J Clin Epidemiol* 2014;**67**:267–77.
132. Terwee CB, Bot SDM, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol* 2007;**60**:34–42.