



## Research article

# Comparative effects of different types of physical activity on health-related quality of life in breast cancer survivors: A systematic review, network meta-analysis, and meta-regression

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## ABSTRACT

**Background:** Physical activity is associated with improved health-related quality of life (HRQoL) in breast cancer survivors (BCS); however, no studies have assessed optimal physical activity.

**Objective:** We aimed to investigate the optimal types of physical activity for improving HRQoL in patients with BCS during and after cancer treatment.

**Methods:** A comprehensive search was conducted in Medline, Embase, Web of Science, and Cochrane Library from inception to November 2023. We included randomized controlled trials (RCTs) reporting the effects of different physical activities on HRQoL in BCS. Two independent reviewers assessed the risk of bias using the Cochrane risk of bias tool for randomized trials (version 2.0). A network meta-analysis approach based on a frequentist framework was used to rank the effectiveness of different physical activities.

**Results:** A total of 66 RCTs with 6464 participants were included. For all BCS, aerobic combined with resistance exercise (CE) (standardized mean difference [SMD] = 0.71; 95 % confidence interval [CI]: 0.40 to 1.10; P-score = 0.75; Grade: moderate) was the most effective physical activity to improve HRQoL. For participants in treatment, resistance exercise (RE) (SMD = 0.68; 95 % CI: 0.35 to 1.10; P-score = 0.84; Grade: moderate) was the most effective. However, after treatment, CE (SMD = 0.77; 95 % CI: 0.28 to 1.26; P-score = 0.74; Grade: very low) remained the most effective way to improve HRQoL in BCS. In addition, the regression analysis did not find any sources of heterogeneity.

**Conclusions:** The findings of this study suggest that all physical activities improved HRQoL in BCS compared to the control group. CE may have the best effect on all survivors and post-treatment survivors, whereas RE has the best effect during treatment. In addition, the quality of the included studies was low, and there was some risk of bias, which may affect the interpretation of the findings.

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## 1. Introduction

Breast cancer (BC) is the leading cause of cancer-related deaths in women and the fifth leading cause of cancer deaths globally, with a high degree of disease heterogeneity, metastasis, and treatment resistance [1,2]. Since the mid-2000s, the incidence of BC in women has been slowly increasing at a rate of 0.5 % per year, and 31 % of newly diagnosed female cancer patients in 2023 were predicted to be BC patients [3]. After peaking in 1989, the mortality rate of female BC declined by 43 %, and the number of breast cancer survivors (BCS) is expected to increase further as a result of advances in medical technology and increased awareness of BC [4]. Maintaining health-related quality of life (HRQoL) in BCS challenges medical and social services.

HRQoL is a term for the health aspect of quality of life, which reflects not only the impact of perceived health on an individual's ability to live a fulfilling life but also that of illness and treatment on disability and daily functioning, and can reflect a patient's sense of well-being [5]. BC treatment, especially chemotherapy, is often accompanied by various side effects, including cardiotoxicity, immune system damage, peripheral neuropathy, and cognitive dysfunction. These direct physical injuries can lead to adverse effects, such as severe depression, weight gain, difficulties with self-management, and secondary lymphedema [6–8]. In addition, patients experience adverse physical and psychological effects long after the end of treatment, which in turn weaken their HRQoL [9]. Therefore, it is particularly important to know how to improve the HRQoL of BC patient prognosis.

The World Health Organization considers all forms of physical activity (PA) to be beneficial to health. PA has gained widespread attention as an essential and beneficial lifestyle [10]. During or after treatment for breast and other cancers, most PAs can have beneficial effects on patients, such as reducing fatigue, decreasing secondary edema, improving physical functioning, regulating mood, and improving psychological well-being, which in turn improves HRQoL [11–14]. However, PA is a term for exercise aggregation that includes all activities in all forms, at any intensity, and for any length of time [15], and Previous studies have treated PA as a single category of exercise, which fails to provide a complete understanding of the effects of interventions in BCS, as well as gives potentially misleading results and exhibits a high degree of heterogeneity, significantly reducing the reliability of the studies [16]. Although another study categorized PA, it was not exhaustive enough in its delineation of activity types, which may have affected patients' judgment in choosing appropriate physical activities. In addition, this study did not specifically analyze BC patients but rather considered all cancer patients as a whole. Therefore, these results do not provide accurate guidance for BC patients when choosing PA [17].

To the best of our knowledge, there is no network meta-analysis (NMA) on the full significance of PA interventions for BCS; therefore, this study quantified the results of randomized controlled trials (RCTs) of PA interventions on HRQoL in BCS and refined the classification of forms of exercise, assessing which forms have the best effect on HRQoL in BCS, in order to cater to the selection of different patients with the optimal PA type. In addition, we divided BC into inter- and post-treatment phases to explore whether there were differences in the effectiveness of the types of PA interventions at different phases to provide evidence that can be used as a reference for clinicians, patients, and caregivers.

## 2. Methods

### 2.1. Protocol registration

This NMA followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension statement for systematic reviews incorporating NMAs for health care (PRISMA-NMA) [18] and the Cochrane Collaboration Handbook [19], and was registered on PROSPERO (CRD 42023474159).

### 2.2. Search strategy

We searched the Medline, Embase, Cochrane Library, and Web of Science databases from inception to November 2023. The language restriction was English, and no restrictions were placed on ethnicity or region of publication. In addition, we used the following Medical Subject Headings (MeSH) and keywords containing Boolean operators: 'breast cancer survivors,' 'exercise,' 'physical activity,' 'yoga,' 'tai chi,' 'qigong,' 'quality of life,' 'health related quality of life,' 'HRQoL,' 'randomized controlled trials.' In addition, the references of previously published reviews and meta-analyses were checked to avoid missing relevant studies. See Appendix page 1 for the detailed search strategy.

### 2.3. Study selection

After excluding duplicate studies, two independent reviewers (Xg N and Tf Y) screened the titles and abstracts against the inclusion and exclusion criteria. A full-text review was performed if the abstract met the inclusion criteria or was unclear. Disagreements were resolved by a third, experienced reviewer (Jb Y). All citations were managed and analyzed using the EndNote X9 software (Thompson ISI Research Soft, USA).

### 2.4. Inclusion and exclusion criteria

The inclusion criteria for this meta-analysis were as follows: (a) population: BCS, and "cancer survivors" is defined from the time of diagnosis and lasting for the balance of life [20]; (b) intervention: any type of exercise intervention, with the exercises categorized into

two levels: the first level (during and after treatment) included aerobic exercise (AE, exercise aimed at improving cardiovascular health), resistance exercise (RE, exercises aimed at improving muscular strength and endurance), combined aerobic and resistance exercise (CE), and mind-body exercise (MBE, exercises aimed at improving physical and mental coordination); in the second level (all BCS), CE and RE remained unchanged, AE was categorized as walking, moderate-intensity continuous exercise (MICE), and aerobic interval exercise (AIT), and MBE was categorized as tai chi (TC), yoga, and qi gong (QG); (c) comparison: non-exercise intervention group, such as usual care, waiting list, and educational consult; (d) outcomes: in order to comprehensively assess the impact of the intervention on the HRQoL in the participants in this study, we used [e.g., Functional Assessment of Cancer Therapy, European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire, and SF-36] as the primary measurement tool. These tools are widely used to assess health status across multiple dimensions of physical, psychological, and social functioning. Each tool was selected based on its validity and reliability in similar studies [21–23]; and (e) study: RCTs.

The exclusion criteria were as follows: (a) patients with diseases other (than BC); (b) intervention studies that combined exercise with medication, diet, or psychotherapy; (c) unavailability of outcome data; and (d) experimental protocols.

## 2.5. Data extraction

Two independent reviewers collected the following data from studies that met the inclusion criteria: (a) author's information; (b) publication date; (c) sample size, age, and disease staging of BC; (d) intervention type, duration, and weekly frequency; and (e) outcomes of interest.

## 2.6. Classification as “during” or “after” breast cancer treatment

First, we analyzed the effects of different exercise interventions on the HRQoL in all BCS. In addition, to explore the benefits of exercise at different periods, we analyzed the effects of exercise on BCS during and after treatment. Patients receiving chemotherapy or radiotherapy as initial treatment for cancer or in the presence of metastasis or recurrence of cancer were defined as “during.” Patients not currently receiving chemotherapy or radiotherapy, or currently receiving endocrine therapy only, were defined as “after.”

## 2.7. Risk of bias and quality of evidence

Two independent reviewers (Xg N and Tf Y) assessed the risk of bias for inclusion in the RCTs using the revised Cochrane Risk of Bias Tool for Randomized Trials (version 2.0) [24]. The tool contains five entries: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of reported results. Studies were categorized as having a low risk of bias, some concerns, or a high risk of bias based on the evaluation results. We used the Recommended Assessment, Development, and Evaluation Grading (GRADE) approach to assess the quality of evidence in the NMA [25].

## 2.8. Measures of treatment effect

The NMA uses the standardized mean difference (SMD) and standard deviation (SD) change from baseline to analyze the effect of PA on HRQoL. If the study did not provide relevant data, standard errors, 95 % confidence intervals (CIs), or p-values were used to calculate SDs [19]. According to the Cochrane Handbook recommendations, if a lower value represents a better study result, the result is multiplied by  $-1$  [19]. If the study is a multi-arm RCT, data will be extracted for all intervention and control groups (CGs). In addition, 0.5 was used as the correlation coefficient to calculate the difference in SD before and after the intervention [26].

## 2.9. Data synthesis

### 2.9.1. Pairwise meta-analyses

First, a paired analysis was conducted using a random effects model. The  $I^2$  statistic was used to test for heterogeneity in the studies, and heterogeneity was considered high when  $I^2$  was  $>50$  % [27]. Publication bias was detected using corrected funnel plots and Egger's test [28].

### 2.9.2. Network meta-analyses

We conducted an NMA of the random effects model in a frequentist framework. First, a network plot was created in which the dots represent the sample size of each intervention, and the dot-to-dot connections represent the number of direct comparisons. Changes in HRQoL were estimated as SMD and 95 % CIs. Forest plots and league tables were produced to represent the extent of the effect of the exercise intervention on HRQoL. We created league tables to show the effect of all exercise interventions on HRQoL and ranked the therapeutic effects of exercise using P-scores [29]. P-scores range from 0 to 1, with higher P-values indicating greater improvements in HRQoL [30]. We assessed network heterogeneity using the  $\tau^2$  and  $I^2$  statistics. We used prediction intervals in all forest plots to better analyze heterogeneity. Network inconsistency was assessed using the node-split method, and network consistency was assessed using a “design-by-treatment” model [31,32].

2.10. Additional analysis

To explore the sources of heterogeneity and validate the model’s stability, we conducted regression analyses with continuous variables of interest, including intervention period, weekly intervention frequency, mean age, year of publication, and duration of a single intervention. In addition, we assumed that the treatment effect was consistent across all interventions. Moreover, we conducted sensitivity analyses that focused on the impact of highly biased studies on the intervention effects.

3. Results

3.1. Study selection and characteristics

A total of 6046 records were identified by searching the electronic databases and retrieving previous studies. After removing duplicates and checking titles and abstracts, 96 full articles were assessed. Of these studies, one was a non-RCT, two had intervention populations that did not meet the inclusion criteria, nine had intervention types that did not meet the inclusion criteria, and eighteen had no available data. Finally, 66 studies were included in the NMA (Fig. 1).

Among the 66 included studies, there were 6464 participants. The participants were all female, and most had disease staging 0–3, with a mean age of 52.38 years. Thirty-seven studies were defined as during treatment and 29 as after treatment. Most of the studies were conducted in North America (25/66, 37.9%), followed by Europe (21/66, 31.8%). The maximum intervention duration was 52 weeks, the minimum was 3 weeks, and the frequency of weekly interventions ranged from one to six. Yoga appeared the most frequently (K = 15), followed by MICE (K = 14), and QG the least (K = 4). The characteristics of the included studies are shown in Appendix 2 (see Appendix 8 for the included literature).

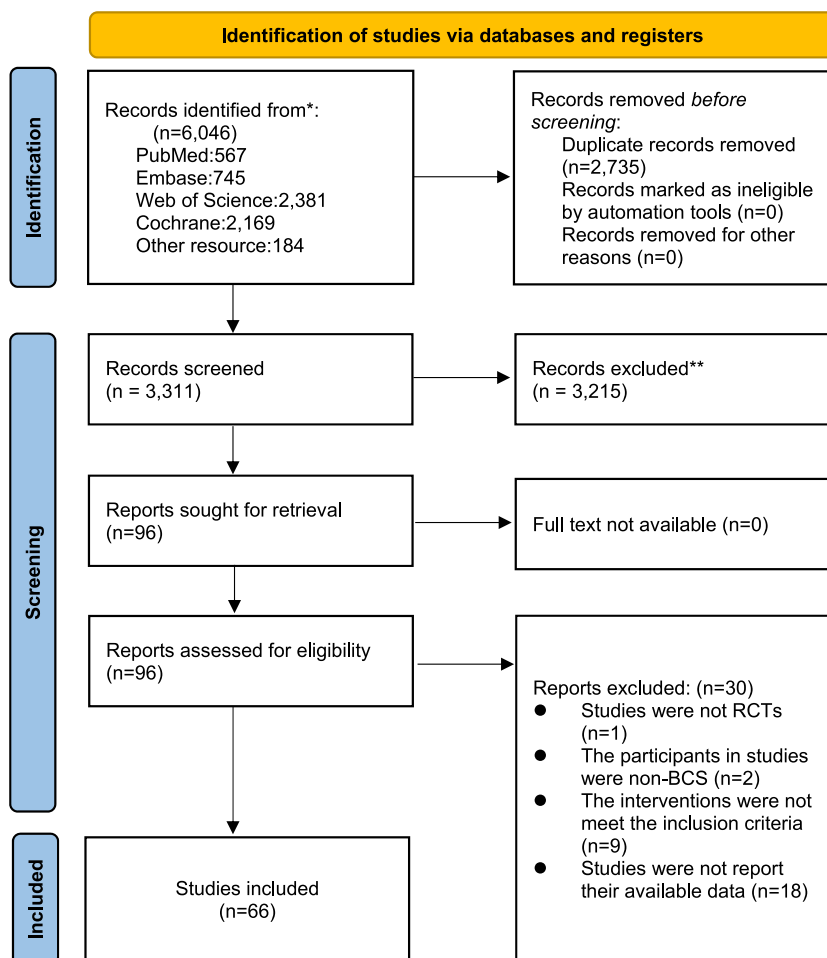


Fig. 1. Literature review flowchart. BCS, breast cancer survivor. RCTs, randomized controlled trials.

### 3.2. Risk of bias and quality of evidence

Of the 66 studies included, 9 were considered to have a high risk of bias, 45 were defined as having some concerns, and 12 had a low risk of bias (Appendix 5). In the NMA, the certainty of evidence was categorized as moderate to very low, with the main reasons for downgrading being risk of bias, imprecision, and inconsistency (Appendix 6).

### 3.3. Pairwise meta-analyses

In the pairwise analysis, compared to the CG, all exercise interventions except high-intensity interval training (HIIT), and TC significantly affected HRQoL (Table 1). There was asymmetry in the funnel plot, and the Egger test result was also less than 0.05, indicating publication bias in the study (Appendix 3).

### 3.4. Network meta-analyses

Fig. 2 shows the network analysis for all BCS. The overall heterogeneity/inconsistency was high ( $I^2 = 82.3\%$  [78.0%; 85.9%];  $\tau^2 = 0.2297$ ). The global Q score for inconsistency was 345.55 ( $p < 0.0001$ ), and significant hotspots of inconsistency were identified in 3 (8.33%) of 36 intervention comparisons, including some disagreements between direct and indirect evidence (Appendix 4). Compared to the CG, CE (SMD = 0.71; 95% CI: 0.40 to 1.10; P-score = 0.75; Grade: moderate) interventions were likely to be most effective, followed by RE (SMD = 0.68; 95% CI: 0.38 to 0.98; P-score = 0.72; Grade: moderate), QG (SMD = 0.69; 95% CI: 0.16 to 1.22; P-score = 0.70; Grade: low), MICE (SMD = 0.61; 95% CI: 0.32 to 0.90; P-score = 0.62; Grade: moderate), HIIT (SMD = 0.56; 95% CI: 0.11 to 1.01; P-score = 0.55; Grade: very low), walking (SMD = 0.52; 95% CI: 0.02 to 1.01; P-score = 0.51; Grade: low), TC (SMD = 0.41; 95% CI: 0.12 to 0.93; P-score = 0.39; Grade: low), and yoga (SMD = 0.30; 95% CI: 0.02 to 0.57; P-score = 0.24; Grade: moderate) (Table 1) (Appendix 6). In addition, the results of the sensitivity analysis were relatively stable (Appendix 7).

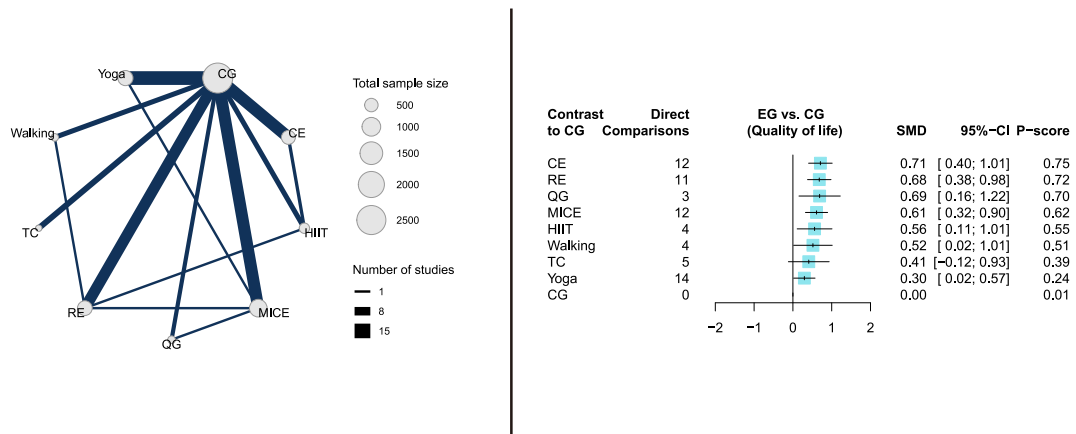
Fig. 3 shows the network analysis of BCS during treatment. The overall heterogeneity/inconsistency was also high ( $I^2 = 80.8\%$  [74.3%; 85.7%];  $\tau^2 = 0.1930$ ). The global Q score for inconsistency was 187.92 ( $p < 0.0001$ ), and no hotspots for inconsistency were identified. Compared to the CG, RE (SMD = 0.68; 95% CI: 0.35 to 1.10; P-score = 0.84; Grade: moderate) interventions were likely to be most effective, followed by CE (SMD = 0.68; 95% CI: 0.38 to 0.98; P-score = 0.72; Grade: moderate), AE (SMD = 0.47; 95% CI: 0.20 to 0.73; P-score = 0.52; Grade: moderate), and MBE (SMD = 0.36; 95% CI: 0.09 to 0.64; P-score = 0.38; Grade: moderate) (Table 2) (Appendix 6). In addition, the sensitivity analysis results were relatively stable (Appendix 7).

Fig. 4 shows the network analysis of BCS after treatment. The overall heterogeneity/inconsistency was also high ( $I^2 = 84.3\%$  [78.1%; 88.8%];  $\tau^2 = 0.3247$ ). The global Q score for inconsistency was 159.56 ( $p < 0.0001$ ), and significant hotspots of inconsistency were identified in 2 (20%) of 10 intervention comparisons, including some disagreements between direct and indirect evidence (Appendix 4). Compared to the CG, CE (SMD = 0.77; 95% CI: 0.28 to 1.26; P-score = 0.74; Grade: very low) interventions were likely to be most effective, followed by AE (SMD = 0.74; 95% CI: 0.34 to 1.14; P-score = 0.72; Grade: moderate), RE (SMD = 0.70; 95% CI: 0.01 to 1.40; P-score = 0.66; Grade: very low), and MBE (SMD = 0.41; 95% CI: 0.03 to 0.80; P-score = 0.36; Grade: very low) (Table 3)

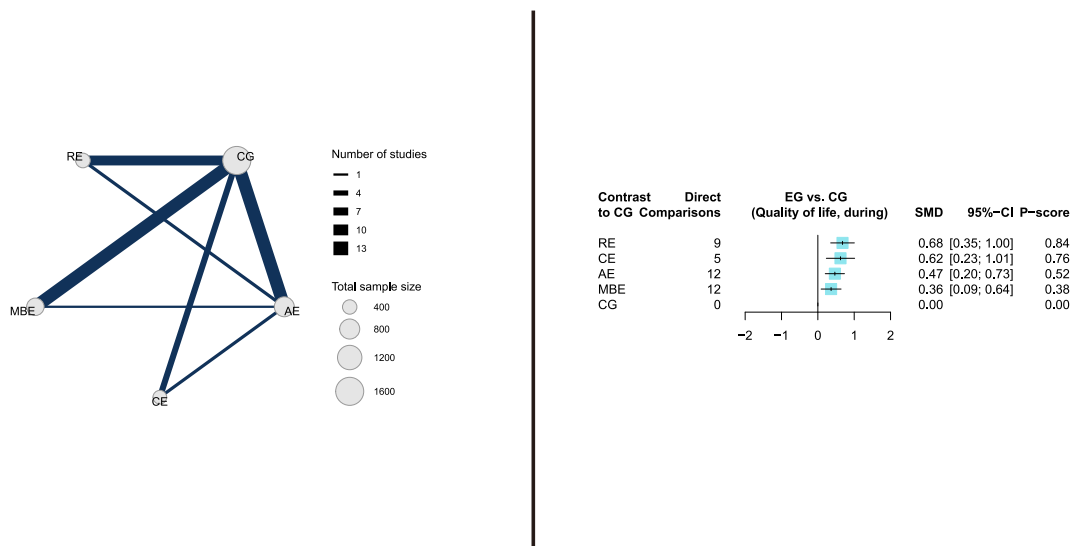
**Table 1**  
Netleague table for all breast cancer survivors.

CE	.	.	.	-0.02 (-0.72, 0.68)	.	.	.	0.73 (0.42, 1.05)
0.03 (-0.40, 0.45)	<b>RE</b>	.	0.00 (-1.12, 1.12)	0.15 (-0.84, 1.14)	<b>1.24 (0.15, 2.33)</b>	.	.	<b>0.57 (0.25, 0.89)</b>
0.02 (-0.59, 0.63)	-0.01 (-0.62, 0.60)	<b>QG</b>	0.27 (-0.79, 1.34)	.	.	.	.	<b>0.63 (0.02, 1.23)</b>
0.10 (-0.32, 0.52)	0.07 (-0.34, 0.48)	0.08 (-0.49, 0.65)	<b>MICE</b>	.	.	.	0.62 (-0.43, 1.67)	<b>0.59 (0.28, 0.90)</b>
0.15 (-0.33, 0.63)	0.12 (-0.40, 0.64)	0.13 (-0.57, 0.83)	0.05 (-0.48, 0.58)	<b>HIIT</b>	.	.	.	0.41 (-0.12, 0.95)
0.19 (-0.39, 0.77)	0.16 (-0.39, 0.71)	0.17 (-0.56, 0.90)	0.09 (-0.48, 0.67)	0.04 (-0.62, 0.71)	<b>Walking</b>	.	.	<b>0.79 (0.24, 1.35)</b>
0.30 (-0.31, 0.91)	0.27 (-0.34, 0.88)	0.28 (-0.47, 1.03)	0.20 (-0.40, 0.80)	0.15 (-0.54, 0.84)	0.11 (-0.62, 0.83)	<b>TC</b>	.	0.41 (-0.12, 0.93)
<b>0.41 (0.00, 0.82)</b>	0.38 (-0.02, 0.79)	0.39 (-0.20, 0.99)	0.31 (-0.07, 0.70)	0.26 (-0.26, 0.79)	0.22 (-0.35, 0.71)	0.11 (-0.48, 0.71)	<b>Yoga</b>	<b>0.32 (0.03, 0.60)</b>
<b>0.71 (0.40, 1.01)</b>	<b>0.68 (0.38, 0.98)</b>	<b>0.69 (0.16, 1.22)</b>	<b>0.61 (0.32, 0.90)</b>	<b>0.56 (0.11, 1.01)</b>	<b>0.52 (0.02, 1.01)</b>	0.41 (-0.12, 0.93)	<b>0.30 (0.02, 0.57)</b>	<b>CG</b>

**Note:** The effects of different physical activity were assessed using a frequency ranking method, and the probability of ranking for each physical activity was expressed as a P-score. Results of the network meta-analysis are presented in the left lower half and results from pairwise comparisons in the upper right half, if available. Comparisons between interventions should be read from left to right and the estimate is in the cell in common between the column-defining intervention and the row-defining intervention. In the left lower half, standard mean differences (SMDs) higher than 0 favor the column-defining intervention, in the upper right half SMDs higher than 0 favor the row defining intervention. Cells in bold print indicate significant results “.” = not available. CE, aerobic combined with resistance exercise. RE, resistance exercise. QG, qi gong. MICE, moderate intensity continuous exercise. HIIT, high intensity interval training. TC, tai chi. CG, control group.



**Fig. 2.** Network plot and forest plot of available comparisons between different exercise interventions on HRQoL in all breast cancer survivors. CE, combined aerobic and resistance exercise. CG, control group. CI, confidence interval. EG, experimental group. HIIT, high intensity interval training. MICE, moderate intensity continuous exercise. QG, qi gong. RE, resistance exercise. SMD standard mean difference. TC, tai chi.



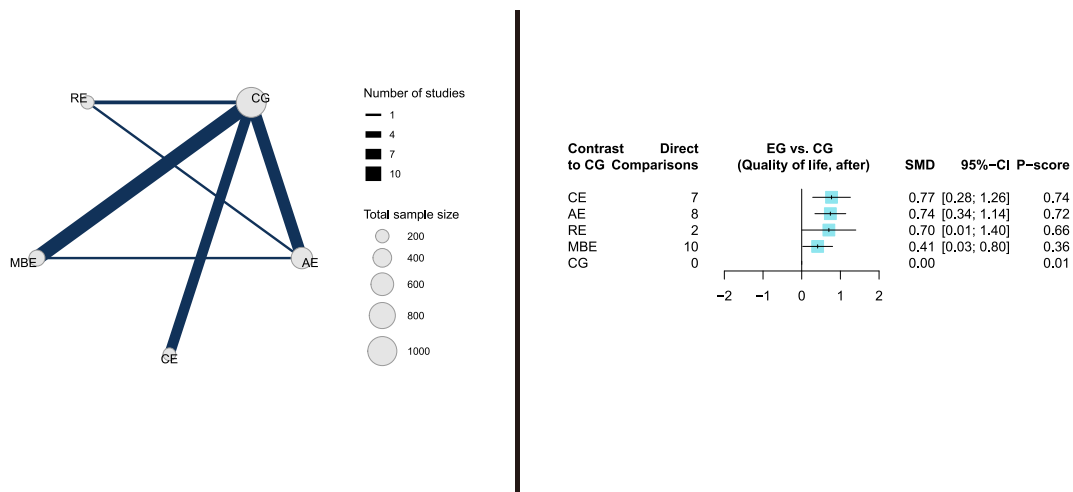
**Fig. 3.** Network plot and forest plot of available comparisons between different exercise interventions on HRQoL in breast cancer survivors (during). AE, aerobic exercise. CE, combined aerobic and resistance exercise. CG, control group. CI, confidence interval. EG, experimental group. MBE, mind-body exercise. RE, resistance exercise. SMD standard mean difference.

**Table 2**

Netleague table for breast cancer survivors (during).

RE	.	0.09 (-0.61, 0.78)	.	0.68 (0.34, 1.01)
0.06 (-0.45, 0.56)	<b>CE</b>	-0.02 (-0.66, 0.63)	.	<b>0.69 (0.25, 1.13)</b>
0.21 (-0.18, 0.61)	0.16 (-0.27, 0.58)	<b>AE</b>	-0.27 (-1.27, 0.72)	<b>0.44 (0.15, 0.73)</b>
0.31 (-0.11, 0.74)	0.26 (-0.21, 0.73)	0.10 (-0.26, 0.47)	<b>MBE</b>	<b>0.33 (0.05, 0.62)</b>
<b>0.68 (0.35, 1.00)</b>	<b>0.62 (0.23, 1.01)</b>	<b>0.47 (0.20, 0.73)</b>	<b>0.36 (0.09, 0.64)</b>	<b>CG</b>

**Note:** The effects of different physical activity were assessed using a frequency ranking method, and the probability of ranking for each physical activity was expressed as a P-score. Results of the network meta-analysis are presented in the left lower half and results from pairwise comparisons in the upper right half, if available. Comparisons between interventions should be read from left to right and the estimate is in the cell in common between the column-defining Intervention and the row-defining Intervention. In the left lower half, standard mean differences (SMDs) higher than 0 favor the column-defining Intervention, in the upper right half SMDs higher than 0 favor the row defining Intervention. Cells in bold print indicate significant results “.” = not available. CE, aerobic combined with resistance exercise. RE, resistance exercise. AE, aerobic exercise. MBE, mind-body exercise. CG, control group.



**Fig. 4.** Network plot and forest plot of available comparisons between different exercise interventions on HRQoL in breast cancer survivors (after). AE, aerobic exercise. CE, combined aerobic and resistance exercise. CG, control group. CI, confidence interval. EG, experimental group. MBE, mind-body exercise. RE, resistance exercise. SMD standard mean difference.

**Table 3**  
Netleague table for breast cancer survivors (after).

CE	.	.	.	0.77 (0.28, 1.26)
0.03 (-0.60, 0.66)	<b>AE</b>	-1.24 (-2.48, 0.01)	0.62 (-0.60, 1.83)	<b>0.86 (0.42, 1.30)</b>
0.07 (-0.78, 0.92)	0.04 (-0.70, 0.78)	<b>RE</b>	.	0.15 (-0.67, 0.97)
0.36 (-0.26, 0.98)	0.33 (-0.20, 0.85)	0.29 (-0.50, 1.08)	<b>MBE</b>	<b>0.44 (0.04, 0.85)</b>
<b>0.77 (0.28, 1.26)</b>	<b>0.74 (0.34, 1.14)</b>	<b>0.70 (0.01, 1.40)</b>	<b>0.41 (0.03, 0.80)</b>	<b>CG</b>

**Note:** The effects of different physical activity were assessed using a frequency ranking method, and the probability of ranking for each physical activity was expressed as a P-score. Results of the network meta-analysis are presented in the left lower half and results from pairwise comparisons in the upper right half, if available. Comparisons between interventions should be read from left to right and the estimate is in the cell in common between the column-defining Intervention and the row-defining Intervention. In the left lower half, standard mean differences (SMDs) higher than 0 favor the column-defining Intervention, in the upper right half SMDs higher than 0 favor the row defining Intervention. Cells in bold print indicate significant results “.” = not available. CE, aerobic combined with resistance exercise. RE, resistance exercise. AE, aerobic exercise. MBE, mind-body exercise. CG, control group.

(Appendix 6). Stability was similarly demonstrated in the sensitivity analyses that excluded studies with a high risk of bias (Appendix 7).

### 3.5. Meta-regression

The regression analysis showed that the intervention period, frequency of intervention, duration of a single intervention session, year of publication, and mean age of the participants were not sources of heterogeneity in this study (Appendix 7).

## 4. Discussion

To the best of our knowledge, this is the first NMA to investigate the effect of PA on the HRQoL in BCS. We pooled 66 RCTs involving 6464 BCS, including eight exercise types, and analyzed them according to the overall, on-treatment, and post-treatment periods. Our study found that the effectiveness of different types of PA varied across different BC periods, with no type of PA exhibiting adverse outcomes. CE showed the best results in the overall and post-treatment periods of BC, whereas RE was the most effective BC treatment. In addition, QG, MICE, HIIT, walking, and yoga had significantly positive effects in the overall phase compared to the CG. RE, CE, AE, and MBE had significant effects during and after treatment. However, it is interesting to note that most effect comparisons between the PAs were similar. According to the GRADE assessment, the quality of evidence was very low (very low to moderate); therefore, the results should be interpreted with caution. Furthermore, the results of the regression analysis suggested that the effects of the exercise interventions in the current study may not have been influenced by the intervention period, frequency of intervention, duration of a single intervention session, year of publication, or mean age of the participants.

HRQoL is a multidimensional concept that includes physical health and social and psychological functioning [33]. The primary scales we extracted were the 36-item Functional Assessment of Cancer Therapy B form (FACT-B), the 36-item Short Form Health Survey of Medical Outcomes (SF-36), and the European Organisation for Research and Treatment of Cancer Quality of Life

Questionnaire (EORTC-QQL-C30). Of these, the FACT-B measures the physical, emotional, social, and functional health of BCS as well as specific issues [34], and the SF-36 contains eight subscales on physical functioning, physical roles, physical pain, general health perceptions, vitality, social functioning, emotional roles, and mental health [35]. The QQL-C30, on the other hand, contains nine multi-item scales, five functional scales (physical, role, cognitive, emotional, and social), three symptom scales (fatigue, pain, nausea, and vomiting), the Global Health and Quality of Life Scale, and several single-item symptom measures [22]. In the overall phase, the effect of PA was significant and not negligible, a finding that is consistent with previous research on the effect of exercise on the quality of life of all cancer patients [36]. The magnitude of the PA type for HRQoL efficacy in BCS was, in order, CE, RE, QG, MICE, HIIT, Walking, TC, Yoga, and CG. However, a fascinating finding was that most PAs did not show significant comparability. However, all of them were better than the CG, suggesting that exercise does not negatively impact HRQoL in BCS, a finding supported by previous studies [37]. Other noteworthy findings were that the effect of CE was significantly better than that of yoga, the efficacy of RE exercise was significantly better than that of walking, and the effect of yoga was the worst, except for the CG, which was also in line with our prediction. The results of a previous study on the effects of yoga on anxiety and depressive symptoms suggested that yoga interventions could significantly improve patients' anxiety symptoms [38]. However, the reported quality of this study was considered very low, and the effects of exercise on HRQoL and psychological well-being in older adults produced only minor to moderate improvements [39]. Although our study ranked PAs, this does not imply that only the highest-ranked type of PA is selected for intervention, and we still recommend that patients choose according to their situation.

Since the PA secondary classification was insufficient for nuanced analysis after dividing the prognostic period of BC, we analyzed it according to the PA primary classification during the treatment and post-treatment periods. We found that PA provided benefits to HRQoL in BCS both during and after treatment, which is consistent with the results of several previous studies [40,41]. An exciting finding when we ranked the results based on improvement in HRQoL was that MBE was the least efficacious among the four PAs compared to the CG. In contrast, the effects of CE, AE, and RE on HRQoL improvement in BCS varied considerably across the different periods of BCS prognosis. During the treatment period, the order of improvement was RE, CE, AE, MBE, and CG in descending order, whereas after the treatment, the order was CE, AE, RE, MBE, and CG. This may be because many cancer cells are still reproducing during the treatment period. Most cells rely on glycolysis to produce energy (the Wahlberg effect) [42,43], and the RE intervention at this time would be more beneficial for inhibiting the activity of cancer cells. After cancer treatment, the number of cancer cells in the body is significantly reduced to the point where there are no longer any cancer cells. Normal cells rely mainly on aerobic oxidation for energy supply and on glycolysis to produce only 30 % of their energy [44]. CE and AE are more conducive to the recovery of body functions. However, among previous studies on the effects of different PA types on HRQoL in all cancers, only some campaigns showed significant efficacy, possibly because of cancer type specificity [17]. Thus, the vast majority of physical activities significantly improved quality of life in BCS, which echoes previous findings on the potential protective effect of PA on BC risk in postmenopausal women [45]. In particular, among postmenopausal women aged 65 years and older, PA showed some preventive effects against BC, which may indirectly enhance the quality of life by improving patients' general health. Although the role of PA in BC prevention was not directly explored in this study, our findings support the direct benefit of exercise in enhancing survivors' quality of life; for example, PA may play a role in postmenopausal women through mechanisms such as modulation of hormone levels and reduction of adipose tissue [46]. It is reasonable to hypothesize that these physiological changes may also positively impact BCS.

#### 4.1. Strengths and limitations

Compared with previous studies, this study has several advantages. First, this study integrated previous studies that only assessed the effect of a single exercise on HRQoL in BCS, compared the efficacy of different PA interventions using NMA, considered the results of direct versus indirect comparisons, improved statistical efficiency, and provided a prioritized ranking of the effect of different PA types on HRQoL in BCS. Second, we used a systematic and comprehensive search strategy to retrieve published studies from an extensive database, with the search not limited by publication date and language, and included studies not restricted to specific types of interventions or comparators. Finally, network meta-regression and sensitivity analyses were performed to fully investigate the sources of heterogeneity in the studies and improve the credibility of the outcomes.

However, this study has several limitations. Although we divided BC into overall, between-treatment, and post-treatment periods, there was still a high degree of heterogeneity in the results of the studies, which we attributed to the variability of the results, one of our most significant limitations. Second, we only included the mean and standard deviation of each study rather than the raw data for each patient, and more precise estimates could be made based on patient-specific data; however, this is beyond our capabilities. Third, because exercise interventions for BCS are unlikely to be blinded, patients in the intervention group may be susceptible to the Hawthorne effect [47] (e.g., patients performing exercise interventions may exhibit behaviors that they perceive as improved because they know that their outcomes will be compared with those of control patients). However, not every exercise type produced the Hawthorne effect in studies that used both types of exercise. Fourth, the current treatment status was not explicitly reported in many studies, and patients varied; therefore, we cannot determine whether patients were homogeneous at the time of the initial intervention. In contrast, the initial disease grade and treatment status may have influenced outcomes [48,49]. Finally, this study failed to generate new hypotheses about the relationship between PA and quality of life, possibly because of limitations in the study design or data processing methods. Future studies should employ more flexible analytical methods, such as machine learning or sophisticated statistical modeling, to reveal deeper patterns and relationships.



## 5. Conclusions

In conclusion, our study suggests that all PA modalities, except TC, may significantly improve the HRQoL in patients with BCS. CE showed the best efficacy in BCS, both overall and in the post-treatment phase, whereas RE was the best option in the mid-treatment phase of BC treatment. However, owing to limited direct evidence, there is no significant difference in efficacy among the various PAs, and individual patient preferences and variability in physical functioning should be fully considered when selecting PA interventions.

### Availability of supporting data

Since all analyses were performed based on previously published studies, no ethical approval or patient consent was required.

### Ethical approval and to participate

Not applicable.

### Consent for publication

Not applicable.

### Availability of supporting data

Since all analyses were performed based on previously published studies, no ethical approval or patient consent was required.

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### CRedit authorship contribution statement

**Xiaogang Nie:** Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Tengfei Yang:** Writing – original draft, Validation, Formal analysis, Data curation. **Xiaoli Nie:** Software, Methodology. **Jinbao Yuan:** Writing – review & editing, Supervision, Data curation, Conceptualization.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.heliyon.2024.e31555>.

## References

- [1] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, et al., Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, *CA A Cancer J. Clin.* 71 (3) (2021) 209–249, <https://doi.org/10.3322/caac.21660>.
- [2] E. Nolan, G.J. Lindeman, J.E. Visvader, Deciphering breast cancer: from biology to the clinic, *Cell* 186 (8) (2023) 1708–1728, <https://doi.org/10.1016/j.cell.2023.01.040>.
- [3] A.N. Giaquinto, H. Sung, K.D. Miller, J.L. Kramer, L.A. Newman, A. Minihan, et al., Breast cancer statistics, 2022, *CA A Cancer J. Clin.* 72 (6) (2022) 524–541, <https://doi.org/10.3322/caac.21754>.
- [4] R.L. Siegel, K.D. Miller, N.S. Wagle, A. Jemal, Cancer statistics, 2023, *CA A Cancer J. Clin.* 73 (1) (2023) 17–48, <https://doi.org/10.3322/caac.21763>.
- [5] K. Haraldstad, A. Wahl, R. Andenæs, J.R. Andersen, M.H. Andersen, E. Beisland, et al., A systematic review of quality of life research in medicine and health sciences, *Qual. Life Res. : an international journal of quality of life aspects of treatment, care and rehabilitation* 28 (10) (2019) 2641–2650, <https://doi.org/10.1007/s11136-019-02214-9>.
- [6] J. Howard-Anderson, P.A. Ganz, J.E. Bower, A.L. Stanton, Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review, *J. Natl. Cancer Inst.* 104 (5) (2012) 386–405, <https://doi.org/10.1093/jnci/djr541>.

- [7] S.C. Gilchrist, A. Barac, P.A. Ades, C.M. Alfano, B.A. Franklin, L.W. Jones, et al., Cardio-Oncology rehabilitation to manage cardiovascular outcomes in cancer patients and survivors: a scientific statement from the American heart association, *Circulation* 139 (21) (2019) e997–e1012, <https://doi.org/10.1161/cir.0000000000000679>.
- [8] S. Pereira, N. Araújo, F. Fontes, L. Lopes-Conceição, T. Dias, A. Ferreira, et al., Cancer-related neuropathic pain, chemotherapy-induced peripheral neuropathy and cognitive decline in a 5-year prospective study of patients with breast cancer-NEON-BC, *Healthcare (Basel, Switzerland)* 11 (24) (2023), <https://doi.org/10.3390/healthcare11243132>.
- [9] A. Shrestha, C. Martin, M. Burton, S. Walters, K. Collins, L. Wyld, Quality of life versus length of life considerations in cancer patients: a systematic literature review, *Psycho Oncol.* 28 (7) (2019) 1367–1380, <https://doi.org/10.1002/pon.5054>.
- [10] F.C. Bull, S.S. Al-Ansari, S. Biddle, K. Borodulin, M.P. Buman, G. Cardon, et al., World Health Organization 2020 guidelines on physical activity and sedentary behaviour, *Br. J. Sports Med.* 54 (24) (2020) 1451–1462, <https://doi.org/10.1136/bjsports-2020-102955>.
- [11] A. Lipsett, S. Barrett, F. Haruna, K. Mustian, A. O'Donovan, The impact of exercise during adjuvant radiotherapy for breast cancer on fatigue and quality of life: a systematic review and meta-analysis, *Breast* 32 (2017) 144–155, <https://doi.org/10.1016/j.breast.2017.02.002>.
- [12] H. Cramer, R. Lauche, P. Klose, S. Lange, J. Langhorst, G.J. Dobos, Yoga for improving health-related quality of life, mental health and cancer-related symptoms in women diagnosed with breast cancer, *Cochrane Database Syst. Rev.* 1 (1) (2017) Cd010802, <https://doi.org/10.1002/14651858.CD010802.pub2>.
- [13] C.M. Dieli-Conwright, K.S. Courneya, W. Demark-Wahnefried, N. Sami, K. Lee, T.A. Buchanan, et al., Effects of aerobic and resistance exercise on metabolic syndrome, sarcopenic obesity, and circulating biomarkers in overweight or obese survivors of breast cancer: a randomized controlled trial, *J. Clin. Oncol. : official journal of the American Society of Clinical Oncology* 36 (9) (2018) 875–883, <https://doi.org/10.1200/jco.2017.75.7526>.
- [14] L.Q. Rogers, K.S. Courneya, P.M. Anton, P. Hopkins-Price, S. Verhulst, S.K. Vicari, 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.* 149 (1) (2015) 109–119, <https://doi.org/10.1007/s10549-014-3216-z>.
- [15] WHO Guidelines Approved by the Guidelines Review Committee, *Global Recommendations on Physical Activity for Health*, World Health Organization, Geneva, 2010. Copyright © World Health Organization 2010.
- [16] D. Aune, G. Markozannes, L. Abar, K. Balducci, M. Cariolou, N. Nanu, et al., Physical activity and health-related quality of life in women with breast cancer: a meta-analysis, *JNCI Cancer Spectr.* 6 (6) (2022), <https://doi.org/10.1093/jncics/pkac072>.
- [17] V. Martínez-Vizcaíno, I. Cervero-Redondo, S. Reina-Gutiérrez, L. Gracia-Marco, J.J. Gil-Cosano, B. Bizzozero-Peroni, 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* 12 (6) (2023) 726–738, <https://doi.org/10.1016/j.jshs.2023.01.002>.
- [18] B. Hutton, G. Salanti, D.M. Caldwell, A. Chaimani, C.H. Schmid, C. Cameron, et al., The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations, *Ann. Intern. Med.* 162 (11) (2015) 777–784.
- [19] J. Higgins, *Cochrane Handbook for Systematic Reviews of Interventions* (2023) [Available from: <https://training.cochrane.org/handbook/current>].
- [20] Survivorship Ncfc, NCCS Presents The State of Cancer Survivorship: 2022 Survey Results U.S.A. <https://canceradvocacy.org/nccs-presents-state-of-cancer-survivorship-2022-survey-results/>, 2022.
- [21] M.J. Brady, D.F. Cella, F. Mo, A.E. Bonomi, D.S. Tulsky, S.R. Lloyd, et al., Reliability and validity of the Functional Assessment of Cancer Therapy-Breast quality-of-life instrument, *J. Clin. Oncol. : official journal of the American Society of Clinical Oncology* 15 (3) (1997) 974–986, <https://doi.org/10.1200/jco.1997.15.3.974>.
- [22] N.K. Aaronson, S. Ahmedzai, B. Bergman, M. Bullinger, A. Cull, N.J. Duez, et al., The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology, *J. Natl. Cancer Inst.* 85 (5) (1993) 365–376, <https://doi.org/10.1093/jnci/85.5.365>.
- [23] J.E. Brazier, R. Harper, N.M. Jones, A. O' Cathain, K.J. Thomas, T. Usherwood, et al., Validating the SF-36 health survey questionnaire: new outcome measure for primary care, *Br. Med. J.* 305 (6846) (1992) 160–164, <https://doi.org/10.1136/bmj.305.6846.160>.
- [24] J.A.C. Sterne, J. Savović, M.J. Page, R.G. Elbers, N.S. Blencowe, I. Boutron, et al., RoB 2: a revised tool for assessing risk of bias in randomised trials, *Br. Med. J.* 366 (2019) 14898, <https://doi.org/10.1136/bmj.14898>.
- [25] R. Brignardello-Petersen, A. Bonner, P.E. Alexander, R.A. Siemieniuk, T.A. Furukawa, B. Rochweg, et al., Advances in the GRADE approach to rate the certainty in estimates from a network meta-analysis, *J. Clin. Epidemiol.* 93 (2018) 36–44, <https://doi.org/10.1016/j.jclinepi.2017.10.005>.
- [26] P. Lopez, R. Radaelli, D.R. Taaffe, R.U. Newton, D.A. Galvão, G.S. Trajano, et al., Resistance Training Load Effects on Muscle Hypertrophy and Strength Gain: Systematic Review and Network Meta-analysis, *Med. Sci. Sports Exerc.* 53 (6) (2021) 1206–1216, <https://doi.org/10.1249/mss.0000000000002585>.
- [27] J.P. Higgins, S.G. Thompson, Quantifying heterogeneity in a meta-analysis, *Stat. Med.* 21 (11) (2002) 1539–1558.
- [28] L. Lin, H. Chu, M.H. Murad, C. Hong, Z. Qu, S.R. Cole, et al., Empirical Comparison of Publication Bias Tests in Meta-Analysis, *J. Gen. Intern. Med.* 33 (8) (2018) 1260–1267, <https://doi.org/10.1007/s11606-018-4425-7>.
- [29] G. Rücker, G. Schwarzer, Ranking treatments in frequentist network meta-analysis works without resampling methods, *BMC Med. Res. Methodol.* 15 (2015) 58, <https://doi.org/10.1186/s12874-015-0060-8>.
- [30] A. Chaimani, J.P. Higgins, D. Mavridis, P. Spyridonos, G. Salanti, Graphical tools for network meta-analysis in STATA, *PLoS One* 8 (10) (2013) e76654, <https://doi.org/10.1371/journal.pone.0076654>.
- [31] S. Dias, N.J. Welton, D.M. Caldwell, A.E. Ades, Checking consistency in mixed treatment comparison meta-analysis, *Stat. Med.* 29 (7–8) (2010) 932–944, <https://doi.org/10.1002/sim.3767>.
- [32] J.P. Higgins, D. Jackson, J.K. Barrett, G. Lu, A.E. Ades, I.R. White, Consistency and inconsistency in network meta-analysis: concepts and models for multi-arm studies, *Res. Synth. Methods* 3 (2) (2012) 98–110, <https://doi.org/10.1002/jrsm.1044>.
- [33] R.M. Kaplan, R.D. Hays, Health-Related Quality of Life Measurement in Public Health, *Annu. Rev. Publ. Health* 43 (2022) 355–373, <https://doi.org/10.1146/annurev-publhealth-052120-012811>.
- [34] D.F. Cella, D.S. Tulsky, G. Gray, B. Sarafian, E. Linn, A. Bonomi, et al., The Functional Assessment of Cancer Therapy scale: development and validation of the general measure, *J. Clin. Oncol. : official journal of the American Society of Clinical Oncology* 11 (3) (1993) 570–579, <https://doi.org/10.1200/jco.1993.11.3.570>.
- [35] R.D. Hays, The medical outcomes study (mos) measures of patient adherence, *J. Behav. Med.* 17 (1994) 361–367.
- [36] L.M. Buffart, J. Kalter, M.G. Sweegers, K.S. Courneya, R.U. Newton, N.K. Aaronson, et al., Effects and moderators of exercise on quality of life and physical function in patients with cancer: An individual patient data meta-analysis of 34 RCTs, *Cancer Treat Rev.* 52 (2017) 91–104, <https://doi.org/10.1016/j.ctrv.2016.11.010>.
- [37] K.H. Schmitz, K.S. Courneya, C. Matthews, W. Demark-Wahnefried, D.A. Galvão, B.M. Pinto, et al., American College of Sports Medicine roundtable on exercise guidelines for cancer survivors, *Med. Sci. Sports Exerc.* 42 (7) (2010) 1409–1426, <https://doi.org/10.1249/MSS.0b013e3181e0c112>.
- [38] J. Martínez-Calderon, M.J. Casuso-Holgado, M.J. Muñoz-Fernandez, C. García-Muñoz, A.M. Heredia-Rizo, Yoga-based interventions may reduce anxiety symptoms in anxiety disorders and depressive symptoms in depressive disorders: a systematic review with meta-analysis and meta-regression, *Br. J. Sports Med.* 57 (22) (2023) 1442–1449, <https://doi.org/10.1136/bjsports-2022-106497>.
- [39] A. Tulloch, H. Bombell, C. Dean, A. Tiedemann, Yoga-based exercise improves health-related quality of life and mental well-being in older people: a systematic review of randomised controlled trials, *Age Ageing* 47 (4) (2018) 537–544, <https://doi.org/10.1093/ageing/afy044>.
- [40] S.I. Mishra, R.W. Scherer, P.M. Geigle, D.R. Berlanstein, O. Topaloglu, C.C. Gotay, et al., Exercise interventions on health-related quality of life for cancer survivors, *Cochrane Database Syst. Rev.* 2012 (8) (2012) Cd007566, <https://doi.org/10.1002/14651858.CD007566.pub2>.
- [41] S.I. Mishra, R.W. Scherer, C. Snyder, P.M. Geigle, D.R. Berlanstein, O. Topaloglu, Exercise interventions on health-related quality of life for people with cancer during active treatment, *Cochrane Database Syst. Rev.* 2012 (8) (2012) Cd008465, <https://doi.org/10.1002/14651858.CD008465.pub2>.
- [42] T.N. Seyfried, L.M. Shelton, Cancer as a metabolic disease, *Nutr. Metab.* 7 (2010) 7, <https://doi.org/10.1186/1743-7075-7-7>.
- [43] J.M. Weiss, The promise and peril of targeting cell metabolism for cancer therapy, *Cancer Immunol. Immunother. : CII.* 69 (2) (2020) 255–261, <https://doi.org/10.1007/s00262-019-02432-7>.

- [44] J. Zheng, Energy metabolism of cancer: Glycolysis versus oxidative phosphorylation, *Oncol. Lett.* 4 (6) (2012) 1151–1157, <https://doi.org/10.3892/ol.2012.928>, submitted for publication.
- [45] K.M. McClain, L.E. McCullough, P.T. Bradshaw, S. Shantakumar, M.B. Terry, A.I. Neugut, et al., Age-Specific Indicators of a Healthy Lifestyle and Postmenopausal Breast Cancer, *J. Wom. Health* 26 (11) (2002) 1176–1184, <https://doi.org/10.1089/jwh.2016.6028>, 2017.
- [46] M. de Roon, A.M. May, A. McTiernan, R. Scholten, P.H.M. Peeters, C.M. Friedenreich, et al., Effect of exercise and/or reduced calorie dietary interventions on breast cancer-related endogenous sex hormones in healthy postmenopausal women, *Breast Cancer Res.* 20 (1) (2018) 81, <https://doi.org/10.1186/s13058-018-1009-8>.
- [47] J. McCambridge, J. Witton, D.R. Elbourne, Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects, *J. Clin. Epidemiol.* 67 (3) (2014) 267–277, <https://doi.org/10.1016/j.jclinepi.2013.08.015>.
- [48] J.A. Ligibel, K. Bohlke, A.M. May, S.K. Clinton, W. Demark-Wahnefried, S.C. Gilchrist, et al., Exercise, Diet, and Weight Management During Cancer Treatment: ASCO Guideline, *J. Clin. Oncol. : official journal of the American Society of Clinical Oncology* 40 (22) (2022) 2491–2507, <https://doi.org/10.1200/jco.22.00687>.
- [49] A.G. Waks, E.P. Winer, Breast Cancer Treatment: A Review, *JAMA* 321 (3) (2019) 288–300, <https://doi.org/10.1001/jama.2018.19323>.