The impact of exercise interventions on domains of quality of life in women diagnosed with breast cancers during chemotherapy treatment: a meta-analytic review

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Summary

Background Exercise can improve quality of life in women undergoing chemotherapy for breast cancer, but evidence of the most effective intervention characteristics remains inconclusive. The aim of this study was to determine the effect of exercise on quality of life in women with breast cancer during chemotherapy and examine whether its relationship varies by described exercise modality, dose, and other study characteristics.

Methods In this systematic review and meta-analysis, a systematic search of five electronic databases (PubMed, Embase, Web of Science, Cochrane Library, and MEDLINE) from Jan 1, 2005, to May 24, 2025, identified randomised controlled trials evaluating exercise interventions and constructs of quality of life in women undergoing chemotherapy for breast cancer. Standardised mean differences (Hedges' g) were calculated and pooled using three-level random-effects models accounting for dependent effect sizes, and potential moderators were examined.

Findings 21 randomised controlled trials (3024 participants) were included. Overall, exercise interventions showed a significant positive effect on constructs of quality of life ($\bar{g}$=0·434 [95% CI 0·272–0·595], p<0·0001). Substantial heterogeneity was observed (I^2=55·76%). Described exercise modality significantly moderated effects (test statistic 3 for moderator differences 28·85, p<0·0001), with aerobic exercise ($\bar{g}$=0·482 [95% CI 0·272–0·595], p<0·0001), combined aerobic-strength training ($\bar{g}$=0·397 [0·156–0·639], p=0·0001), and strength-alone ($\bar{g}$=0·335 [0·002–0·669], p<0·049) showing significant benefits. This study is retrospectively registered with PROSPERO (CRD420251044479).

Interpretation Exercise interventions significantly affect quality of life in women with breast cancer during chemotherapy. Aerobic and combined aerobic–strength training both showed significant benefits. Further research is needed to establish optimal exercise prescriptions.

Funding None.

Lancet Healthy Longev 2026

Published Online
https://doi.org/10.1016/j.lanhl.2026.100819

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Introduction

Worldwide, breast cancer is the most commonly diagnosed cancer in women, with treatment typically including surgery, radiation, systemic therapies, and hormonal therapies.[1–4] Although these treatments have improved rates of survival, they often lead to substantial decreases in quality of life due to treatment and cancer-related side-effects, including fatigue, pain, decreased physical function, and psychological distress.[5–8] Exercise is proposed as a non-pharmacological intervention that could mitigate adverse effects and improve quality of life during treatment.[6,9–11] The existing literature on exercise for people with cancer has grown substantially in recent years, with numerous trials examining various exercise modalities (aerobic, resistance, and a combination) and doses, and recent American Society of Clinical Oncology and American Cancer Society guideline updates in 2022.[12,13] Quality of life was selected as the primary outcome because it is a central patient-reported outcome during chemotherapy and previous evidence shows that exercise can affect quality of life domains differently across trials.

This meta-analysis focuses exclusively on women, as female breast cancer has unique biological characteristics (90% of individuals express hormone receptors and 18% are HER2 positive) that affect treatment response, requiring targeted therapies that interact differently with exercise interventions.[14,15] In contrast, male breast cancer accounts for less than 1% of all breast cancer cases and presents with different prognostic factors, treatment algorithms, and physiological responses to therapy.[16,17]

Chemotherapy was selected as the treatment modality for this study because it represents the most systemically toxic cancer treatment, creating the greatest need for supportive interventions and presenting unique challenges for exercise implementation and uptake. Unlike radiation therapy, immunotherapy, or surgery, chemotherapy induces cyclical systemic toxicity that affects multiple organ systems simultaneously and can cause acute neutropenia and cumulative cardiotoxicity, which demand adaptable exercise protocols.[18–21]

Past studies have shown that exercise during chemotherapy uniquely targets acute, treatment-related toxicities

Research in context

Evidence before this study

Five electronic databases (PubMed, Embase, Web of Science, Cochrane Library, and MEDLINE) were systematically searched from Jan 1, 2005, to May 24, 2025, using the Population, Intervention, Comparison, Outcome framework (population: women with breast cancer undergoing chemotherapy; intervention: exercise; comparison: standard care; outcome: quality of life). Our search strategy combined four concept areas using Boolean operators: disease terms (breast cancer, and breast neoplasm); treatment terms (chemotherapy, and adjuvant therapy); intervention terms (exercise, physical activity, resistance training, and aerobic exercise); and outcome terms (quality of life, QoL, FACT, and EORTC). An example search string is: (("breast cancer" OR "breast neoplasm") AND ("chemotherapy" OR "adjuvant therapy") AND ("exercise" OR "physical activity" OR "resistance training" OR "aerobic exercise") AND ("quality of life" OR "QoL" OR "FACT" OR "EORTC")). The database search yielded 8116 records (415 from PubMed, 676 from Embase, 3305 from Web of Science, 2324 from Cochrane Library, and 1396 from MEDLINE). Previous evidence suggests that exercise could improve quality of life in people with cancer, although trials have shown variable effects across quality of life domains.

Added value of this study

Unlike studies focusing on post-treatment or mixed (during and post-treatment) populations, this meta-analysis assessed 21 randomised controlled trials involving 3024 women undergoing chemotherapy for breast cancer. Exercise improved quality of life during active treatment (g=0·43), with positive findings consistent across exercise modalities.

Implications of all the available evidence

Current evidence supports exercise during chemotherapy for breast cancer to improve quality of life. Aerobic, resistance-only, and combined programmes can all be recommended, allowing individualised approaches aligned with American Society of Clinical Oncology guidelines.

See Online for appendix

such as fatigue, functional decline, and cardiometabolic dysregulation, producing effects that differ in magnitude and mechanism from post-treatment exercise.[22–25] The American Society of Clinical Oncology recommends that oncology providers encourage regular aerobic and resistance exercise during active treatment with curative intent to mitigate treatment-related side-effects.[12] However, questions remain about the optimal exercise prescription during chemotherapy regarding which described exercise modality (aerobic, resistance, or combinations thereof) yields the greatest quality of life benefits, and how to integrate exercise into oncology care models alongside active chemotherapy.[26] Additionally, heterogeneity in study designs (described exercise modality, treatment types, or chemotherapy regimens), numerous varied validated quality of life measures, and differences in populations have made it challenging to draw definitive conclusions about the effectiveness of exercise interventions on quality of life, specifically during chemotherapy for breast cancer.[27–29]

Hence, our primary research question was: among women diagnosed with breast cancer undergoing chemotherapy, how effective is exercise compared with standard care or no exercise intervention in improving quality of life? This meta-analysis addresses a notable gap in the literature by focusing specifically on women undergoing chemotherapy rather than on those who have survived cancer after active treatment.

Methods

Search strategy and selection criteria

A comprehensive systematic search was done from Jan 21, 2025, to May 24, 2025, following PRISMA guidelines.[30] Full search strategies using the Population, Intervention, Comparison, Outcome (PICO) framework for all databases are provided in the appendix (pp 41–43) for reproducibility. Five electronic databases were systematically searched: PubMed, Embase, Web of Science, Cochrane Library, and MEDLINE. These databases were selected to provide comprehensive coverage of peer-reviewed biomedical literature. Search terms were developed using the PICO framework and included controlled vocabulary and free-text terms related to breast cancer, exercise interventions, and quality of life outcomes.[31] Articles were restricted to publication dates Jan 1, 2005, to May 24, 2025, to capture the most recent exercise oncology findings, species (humans), sex (female), language (English), and article type (clinical trial or randomised controlled trial). Duplicates were identified and removed using Zotero.

Articles were included if they met the following criteria: population—women diagnosed with breast cancer undergoing active chemotherapy; intervention—exercise programmes (aerobic, strength or resistance, or combined); comparison—standard care or no exercise; outcome—validated quality of life questionnaire measures; study design—randomised controlled trials; publication date—Jan 1, 2005, to May 24, 2025; and language—English (regardless of where published). Exclusion criteria were: individuals assigned male at birth; studies focusing solely on post-treatment survivorship; cancer prevention studies; studies focusing only on laboratory markers without patient-reported outcomes; non-peer-reviewed publications; animal studies; studies without separate breast cancer results; studies without a control group; insufficient statistical data for effect size and SE calculation; multicomponent interventions (eg, diet and exercise); duplicate data from other included studies; and studies where

chemotherapy was not administered during the intervention, or included both male and female participants without results being reported separately.

Title and abstract screening was assisted by SWIFT-Review (Sciome, Research Triangle Park, NC, USA). This semi-automated screening tool uses machine learning to prioritise records likely to meet inclusion criteria.[32] Records with SWIFT-Review scores of 0·73 or higher were advanced to full-text assessment, and all records scoring below 0·73 underwent manual title and abstract screening to ensure that no relevant studies were excluded on the basis of prioritisation scores alone. Several articles initially met our inclusion criteria but were excluded because they did not provide comprehensive, longitudinal quality of life data from baseline through to the completion of chemotherapy, nor did they include a validated, general quality of life outcome metric (eg, Functional Assessment of Cancer Therapy, European Organisation for Research and Treatment of Cancer, or Short-Form 36 surveys). A complete list of excluded articles with reasons is available upon request.

This study is retrospectively registered with PROSPERO (CRD420251044479).

Variables and classifications

Study characteristics (author, year, and country), intervention protocols, assessment methods, and sample characteristics were extracted from each study. Countries were grouped into regions (North America, Europe, Asia, and Other; appendix pp 2–36). Exercise interventions were classified into aerobic exercise, strength or resistance training, and combined (appendix p 37). Quality of life domains were categorised into global quality of life, psychosocial, and physical (appendix p 37). The quality of life timepoint reflects the assessment nearest to chemotherapy or exercise intervention completion used for effect-size extraction.

Inter-rater reliability

Data verification and extraction using a standardised form, as well as title and abstract review, were done by independent reviewers (LDR and EMM). Inter-rater reliability measured by Cohen's κ coefficient was 0·80 (calculated from agreement on include and exclude decisions during title and abstract screening), indicating substantial agreement between reviewers. Discrepancies were resolved through discussion until consensus was reached. Full texts were then assessed against inclusion and exclusion criteria, with a third reviewer (TEC) resolving disagreements.

Effect size and SE

Effect sizes were calculated using Hedges' g, representing the standardised mean difference between intervention and control groups, with a correction for small sample bias. Hedges' g was used to quantify standardised mean differences, with 0·20 interpreted as a small effect, 0·50 as medium, and 0·80 as large. To aid interpretation, these values were also expressed as Cohen's U_3, such that standardised mean differences of 0·20, 0·50, and 0·80 corresponded to approximately 58%, 69%, and 79% of the intervention group scoring above the control group mean, respectively, assuming normally distributed outcomes with equal variances.[33,34] Effect sizes and their associated SEs were calculated using the metafor package in R (version 4.1.0), using post-intervention measurements collected at or closest to chemotherapy completion.[35] For articles reporting multiple commonly used quality of life outcomes, separate effect sizes were calculated for each instrument. When studies examined multiple described exercise modalities, effect sizes were calculated separately for each intervention type. Directionality was standardised, so positive values indicated quality of life improvements with exercise.

Bias assessment

Study quality was evaluated using the Cochrane Risk of Bias 2 tool, assessing five domains: randomisation process, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting.[36]

Publication bias was assessed using visual inspection of funnel plots for asymmetry, and Rosenthal's fail-safe N to determine the number of null studies needed to nullify the observed effect. Results were considered robust if the fail-safe N exceeded 5k + 10, where k is the number of studies.

Certainty of evidence for the primary outcome (quality of life) was assessed using the GRADE approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Data analysis

We carried out a three-level random-effects meta-analysis using the metafor package in R (version 4.1.0). This hierarchical structure accounts for sampling variance (Level 1), within-study variance between multiple outcomes (Level 2), and between-study variance (Level 3), which appropriately handles the dependency arising from multiple effect sizes extracted from the same study. When studies included multiple intervention groups sharing a control group, all corresponding effect sizes were modelled together under the same study identifier, allowing the shared control dependence to be modelled at Level 2. To ensure the robustness of our primary three-level model, we compared its results against alternative approaches: a traditional two-level model, robust variance estimation (ρ=0·8), and the three-level model incorporating cluster-robust SEs.[37–40]

Heterogeneity was quantified using partitioned I^2 statistics (Level 2 I^2, Level 3 I^2, and Total I^2). Subgroup analyses examined described exercise modality, quality of life domain, and geographical region using three-level metaregression with cluster-robust SEs. Moderator significance was assessed with the test statistic for moderator differences (Q_M), and R^2 values quantified the proportion of between-study heterogeneity explained. Post-hoc pairwise comparisons of significant moderator levels were

conducted using Bonferroni-adjusted p values. Finally, sensitivity analyses included influence diagnostics (Cook's distances >1) and model robustness assessment.

Role of the funding source

There was no funding source for this study.

Results

Across five electronic databases we found a total of 8116 records (figure 1). After duplicates were removed, 2968 records remained for screening with 50 records screened for eligibility via full text assessment. The meta-analysis incorporated 49 effect sizes from 21 individual randomised controlled trials reported in 22 manuscripts published between 2007 and 2025, representing a total sample size of 3024 participants (for full list see appendix pp 2–36). There were 22 manuscripts and 21 independent studies because the OptiTrain trial data were reported in two separate publications, which were treated as a single study to avoid double counting.[11,23]

Studies contributed multiple effect sizes to the meta-analysis through three primary mechanisms. First, many studies assessed multiple quality of life domains using different validated instruments, such as separate measures for global quality of life, physical functioning, and psychological wellbeing. For instance, Gokal and colleagues reported outcomes for both psychosocial and physical domains using different subscales.[41] Second, several trials included multiple intervention groups compared against a single control group. Van Waart and colleagues exemplify this design, comparing both OnTrack and Onco-Move exercise interventions with standard care.[42] Third, some studies employed multiple assessment instruments to capture different aspects of quality of life, as shown by Sturgeon and colleagues who used various Short-Form 36 subscales to comprehensively assess health-related quality of life.[43] The average number of effect sizes per study was 2·33. By described exercise modality, interventions comprised aerobic exercise (k_{effect}=28), combined training (k_{effect}=18), and strength training alone (k_{effect}=3).

The three-level random-effects meta-analysis showed a statistically significant positive effect of exercise interventions on quality of life with an overall effect size of 0·434 (95% CI 0·272–0·595, p<0·0001; figure 2). Substantial heterogeneity was observed across studies with a total I^2 of 55·8%. The heterogeneity decomposition indicated that 100% of total variance was attributable to within-study differences (Level 2 I^2=55·8%) and 0% to between-study differences (Level 3 I^2=0%), with the remainder (44·2%) due to sampling error. Within-study τ^2 was 0 and between-study τ^2 was 0·086.

To examine whether our findings were sensitive to this modelling choice, we did three sensitivity analyses (table 1). The first analysis was a traditional two-level model ($\bar{g}$=0·435 [95% CI 0·272–0·595]) that incorrectly assumes independence between effect sizes, which we expected would underestimate SE and produce narrower CIs. The second analysis was a robust variance estimation ($\bar{g}$=0·434 [0·272–0·595]) using ρ=0·80, which provides valid inference even with model misspecification but is less statistically efficient than the three-level model when the hierarchical structure is correctly specified. For the third analysis, we applied cluster-robust SE to our three-level model ($\bar{g}$=0·434 [0·272–0·595]) to address potential small-sample bias with 21 studies. All sensitivity analyses showed the consistent inference as our primary finding of a positive effect

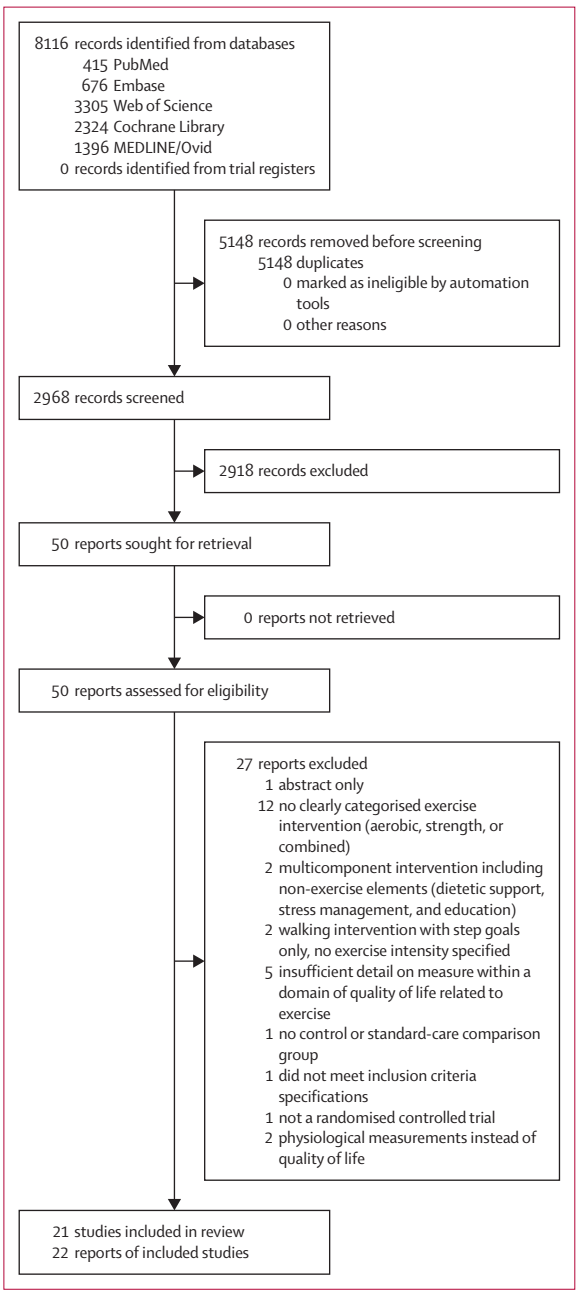

Figure 1: **Study selection**

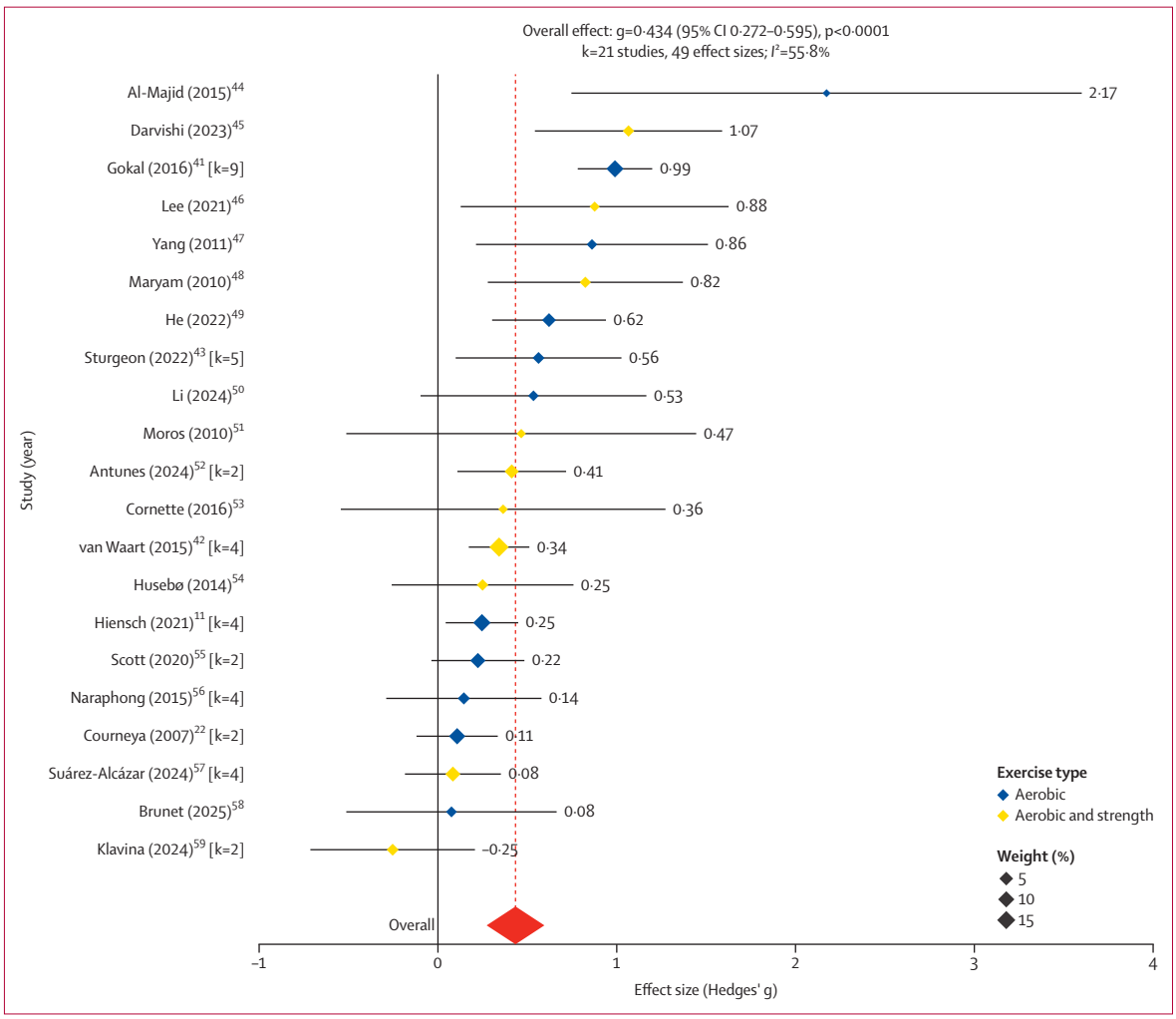

Figure 2: **Forest plot of effects of exercise on quality of life**

Each study is represented by a single summary effect size, calculated as the inverse variance weighted mean of all effects from that study. Studies contributing multiple effect sizes are indicated by [k=n], where n is the number of effects. The red diamond represents the overall pooled effect with 95% CI. Point sizes reflect study weights in the meta-analysis.

($\bar{g}$=0·434). These results show that the beneficial effect of exercise on quality of life is not an artifact of our analytical approach.

Risk of bias evaluation revealed generally high methodological quality across included studies. Overall risk of bias was low in 12 (55%) studies[11,22,23,42,46,47,49,52,53,55,58,59] and showed some concerns in ten (45%) studies,[41,43–45,48,50,51,54,56,57,60] with no studies rated as high risk across all domains. For randomisation, 16 (73%) studies showed low risk and six (27%) showed some concerns. Missing outcome data showed low risk in 15 (68%) studies and some concerns in seven (32%) studies. All studies showed low risk for intervention deviations, outcome measurement, and selective reporting (appendix p 39).

Visual inspection of the funnel plot revealed a relatively symmetrical distribution of effect sizes around the overall mean effect, with studies distributed across all levels of precision (appendix p 40). The plot showed no obvious asymmetry that would suggest publication bias, although there was some scatter among smaller studies (higher SE). Rosenthal's fail-safe N analysis indicated that 89 null studies would be needed to nullify the observed effect, which exceeded the criterion of 115 (5k + 10, where k=21), suggesting that the results are robust to publication bias.

Using the GRADE approach, the certainty of evidence for the pooled quality of life effect was rated as moderate. This rating reflects the overall low risk of bias and consistent direction of benefit across studies, with a conservative downgrade due to variation in quality of life measurement instruments.

Per the mixed-effects meta-regression using the three-level model with cluster-robust SE, the described exercise modality emerged as a significant moderator (Q_M[3]=28·85, p<0·0001), explaining the substantial heterogeneity

	Number of studies	Number of effects	Estimate $\bar{g}$ (95% CI)	SE	p value	I^2 (%)	Within-study τ^2	Between-study τ^2
Two-level model	21	49	0·435 (0·272–0·595)	0·082	<0·0001	..	..	73·8
Three-level model*	21	49	0·434 (0·272–0·595)	0·082	<0·0001	55·8%	0	55·8
Robust variance estimation (ρ=0·80)	21	49	0·434 (0·272–0·595)	..	<0·0001	..	..	..
Cluster-robust model	21	49	0·434 (0·260–0·607)	0·082	<0·0001	..	..	..

*Primary analysis model.

Table 1: **Model comparison and robustness assessment**

	$\bar{g}$ (95% CI)	SE	p value	Q_M	p value
Exercise modality					
Aerobic	0·482 (0·262 to 0·703)	0·113	<0·0001*	28·85	<0·0001*
Aerobic & Strength	0·397 (0·156 to 0·639)	0·123	0·0001*	28·85	<0·0001*
Strength	0·335 (0·002 to 0·669)	0·17	0·049*	28·85	<0·0001*
Quality of life domain					
Functional	0·205 (–0·199 to 0·609)	0·206	0·32	33·37	<0·0001*
Global quality of life	0·419 (0·235 to 0·603)	0·094	<0·0001*	33·37	<0·0001*
Mental health	0·584 (0·240 to 0·927)	0·175	0·0001*	33·37	<0·0001*
Physical health	0·496 (0·286 to 0·706)	0·107	<0·0001*	33·37	<0·0001*
Geographical region					
Asia	0·656 (0·335 to 0·977)	0·164	<0·0001*	29·05	<0·0001*
Europe	0·321 (0·062 to 0·581)	0·132	0·015*	29·05	<0·0001*
North America	0·395 (0·070 to 0·721)	0·166	0·017*	29·05	<0·0001*
Other	0·413 (–0·259 to 1·084)	0·343	0·23	29·05	<0·0001

*p<0·05. Q_M=test statistic for moderator differences. $\bar{g}$ represents the pooled standardised mean difference within each subgroup. Post-hoc pairwise comparisons of subgroup coefficients were done for exercise modality and exercise dose, with three contrasts tested in each moderator. Bonferroni-adjusted p values were non-significant for all pairwise comparisons, indicating no statistically reliable differences between subgroups after correction for multiple testing.

Table 2: **Moderator analysis results**

(table 2). Aerobic exercise showed statistically significant benefits with $\bar{g}$= 0·482 (95% CI 0·262–0·703, p<0·0001), as did combined training with $\bar{g}$=0·397 (0·156–0·639, p<0·0001), and strength training with $\bar{g}$=0·335 (0·002–0·669, p=0·050). Post-hoc pairwise comparisons with Bonferroni adjustment revealed no significant differences between any described exercise modalities.

Quality of life domain categories were significantly different (Q_M[4]=33·37, p<0·0001). All domain categories besides functional ($\bar{g}$=0·205 [95% CI –0·199 to 0·609, p=0·32]) showed significant positive effects, with global quality of life showing $\bar{g}$=0·419 (0·235–0·603, p<0·0001), mental health showing $\bar{g}$=0·584 (0·240–0·927, p=0·0001), and physical showing $\bar{g}$=0·496 (0·286–0·706, p<0·0001). Post-hoc pairwise comparisons indicated no significant differences between regions after Bonferroni adjustment.

Significant regional variations were identified (Q_M[4]=29·05, p<0·0001). Asian studies had the largest effect sizes with $\bar{g}$=0·656 (95% CI 0·335 to 0·977, p<0·0001), followed by North American with $\bar{g}$=0·395 (0·070 to 0·721, p=0·017), Other (Brazil) with $\bar{g}$=0·413 (–0·259 to 1·084, p=0·23), and European with $\bar{g}$=0·321 (0·062 to 0·581, p=0·015). Post-hoc pairwise comparisons indicated no significant differences between regions after Bonferroni adjustment.

The distribution of effect sizes varied considerably by modality. Three notable outliers were identified: Al-Majid and colleagues with $\bar{g}$=2·17,[44] Darvishi and colleagues with $\bar{g}$=1·07,[45] and Klavina and colleagues with $\bar{g}$=–0·256.[59] The violin plot analysis (appendix p 40) revealed that aerobic interventions showed the most variable effect.

Visual inspection of the funnel plot revealed a relatively symmetrical distribution of effect sizes around the overall mean effect, with studies distributed across all levels of precision. The plot showed no obvious asymmetry that would suggest publication bias. Rosenthal's fail-safe N analysis indicated that 89 null studies would be needed to nullify the observed effect, which exceeded the criterion of 115 (5k + 10, where k=21), suggesting that the results are robust to publication bias.

Discussion

This meta-analysis indicated that exercise interventions have a statistically significant positive impact on quality of life in women with breast cancer undergoing chemotherapy.

The overall effect size was 0·434, which translates to approximately 66% likelihood that a randomly selected participant in the exercise group will report better quality of life than a randomly selected participant receiving standard care alone. The consistency of this effect across four different analytical approaches (three-level, robust variance estimation, cluster-robust, and traditional two-level models) shows the robustness of our findings. The substantial heterogeneity observed (I^2=55·8%) was expected given the diversity of exercise modalities and outcome measures included. The three-level model clarified the structure of this variation by showing that none of the heterogeneity arose from within-study outcome clustering, and all measurable heterogeneity reflected differences between studies.

The findings ($\bar{g}$=0·434) align with the moderate beneficial effects found by Buffart and colleagues[9] and Lahart and colleagues,[61] and the consistent benefits during and after treatment found by Spence and colleagues.[62] Multiple mechanisms explain exercise benefits during chemotherapy: anti-inflammatory effects as exercise triggers muscle-derived IL-6 release, initiating anti-inflammatory cascades that reduce systemic inflammation contributing to fatigue, pain, and distress[63,64]; neuroendocrine regulation through endogenous opioid release, providing analgesia and mood

enhancement; and normalisation of hypothalamic–pituitary–adrenal axis function, reducing cortisol dysregulation and improving stress resilience.[65] These mechanisms can result in acute responses and could explain domain-specific benefits.

Described exercise modality emerged as a significant moderator ($Q_M[3]=28{\cdot}85$, $p<0{\cdot}0001$), with all three modalities (aerobic exercise, combined aerobic–strength training, and strength training alone) showing significant benefits. However, post-hoc pairwise comparisons with Bonferroni adjustment revealed no significant differences between any modalities, indicating similar effectiveness.

This meta-analysis has several limitations. Substantial heterogeneity ($I^2=55{\cdot}8\%$) indicates that unmeasured factors continue to shape exercise effects on quality of life. Clinical moderators such as age, tumour stage, and subtype could not be examined because these characteristics were reported inconsistently across trials. Adherence was documented in approximately half of the studies and captured with heterogeneous methods, limiting its value as a potential moderator. The greater variability observed in aerobic intervention effects probably reflects differences in programme design, supervision, and progression, and physiological outcomes were not reported consistently enough to evaluate whether physiological changes contributed to quality of life improvements. Variation in quality of life instruments across studies might introduce measurement bias, although the use of standardised effect sizes helps to mitigate this concern. Global quality of life scores were not consistently available, requiring reliance on subdomain outcomes and a three-level model to account for dependence among effect sizes. The small number of strength-based trials restricts the generalisability of those findings, and the geographical clustering of studies in high-income countries could constrain broader applicability.

The significant regional differences in effect sizes ($Q_M[4]=29{\cdot}05$, $p<0{\cdot}0001$) highlight important considerations for global implementation of exercise interventions. Asian studies had the largest effects ($\bar{g}=0{\cdot}656$), which might reflect differences in health-care systems, cultural attitudes towards exercise, implementation fidelity, or population characteristics. These variations underscore the importance of culturally adapted and contextually appropriate exercise interventions. However, these regional findings should be interpreted with caution, as our analysis was restricted to English-language publications. Studies published in other languages from both European and Asian contexts might have been excluded, potentially influencing the observed regional differences.

These findings are consistent with American Society of Clinical Oncology recommendations.[66] Clinicians should consider recommending both aerobic exercise and combined aerobic–strength exercise. The variability in aerobic effects reflects heterogeneity in prescription parameters (appendix pp 41–43), which can potentially speak to differences in modality reports, which can create overlap with aerobic and resistance training. Future studies need standardised quantification using frameworks like the Consensus on Exercise Reporting Template to enable stronger dose–response conclusions.[67,68]

Future studies should investigate biological and psychological mechanisms underlying modality-specific effects and examine optimal delivery models, adherence strategies, and pathways for integrating exercise into oncology care. Exercise goals in oncology are multifactorial and might require different prescriptions with varying intensity demands. Although improving quality of life is important, exercise ultimately aims to improve long-term morbidity and mortality. Future research should examine whether integrated prescriptions optimise across domains simultaneously or whether sequential approaches (symptom management during treatment or functional restoration after treatment) prove more effective.

Contributors

LDR conceptualised the study, did the systematic search, did title and abstract screening, extracted data, did all statistical analyses, interpreted results, and wrote the first draft of the manuscript. SA supervised the study and provided expertise in meta-analytic methodology and data analysis. EMM did independent data extraction and verified the underlying data along with LDR. MW, LY, and CJC contributed to critical revision of the manuscript for important intellectual content. SHLG provided supervision throughout the study and made critical revisions of the manuscript. KHS provided supervision and contributed subject matter expertise in exercise oncology. TEC provided primary mentorship throughout all phases of the study, contributed to the first draft, supervised the study design and conduct, critically revised all versions of the manuscript, and resolved disagreements during study selection. LDR and EMM accessed and verified the underlying data. All authors reviewed and approved the final version of the manuscript, had access to all of the study data, and were responsible for the final decision to submit for publication.

Declaration of interests

KHS reports fees from FKlose Training and Consulting. All other authors declare no competing interests.

Data sharing

The data extraction form, complete dataset of extracted data, and R code used for analyses are available from the corresponding author (LDR) upon reasonable request by email.

Acknowledgments

None.

References

1 Bashar MA, Begam N. Breast cancer surpasses lung cancer as the most commonly diagnosed cancer worldwide. *Indian J Cancer* 2022; **59:** 438–39.
2 Wilkinson L, Gathani T. Understanding breast cancer as a global health concern. *Br J Radiol* 2022; **95:** 20211033.
3 Harbeck N, Penault-Llorca F, Cortes J, et al. Breast cancer. *Nat Rev Dis Primer* 2019; **5:** 66.
4 Arnold M, Morgan E, Rumgay H, et al. Current and future burden of breast cancer: global statistics for 2020 and 2040. *Breast* 2022; **66:** 15–23.
5 Costanzo ES, Lutgendorf SK, Mattes ML, et al. Adjusting to life after treatment: distress and quality of life following treatment for breast cancer. *Br J Cancer* 2007; **97:** 1625–31.
6 Zhan Y, Feder SL, Lustberg M, Batten J, Knobf MT. Health-related quality of life in women with metastatic breast cancer: an integrative review. *J Adv Nurs* 2024; **81:** 3485–503.
7 Reimer T, Gerber B. Quality-of-life considerations in the treatment of early-stage breast cancer in the elderly. *Drugs Aging* 2010; **27:** 791–800.

8 Mokhtari-Hessari P, Montazeri A. Health-related quality of life in breast cancer patients: review of reviews from 2008 to 2018. *Health Qual Life Outcomes* 2020; **18:** 338.

9 Buffart LM, Kalter J, Sweegers MG, 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* 2017; **52:** 91–104.

10 Piringer G, Holzner B, Mayrbaeurl B, et al. Influence of a structured exercise training on patients reported quality of life in colorectal cancer patients after adjuvant chemotherapy: a pilot study. *Integr Cancer Ther* 2020; published online July 31. https://doi.org/10.1177/1534735420938458.

11 Hiensch AE, Mijwel S, Bargiela D, Wengström Y, May AM, Rundqvist H. Inflammation mediates exercise effects on fatigue in patients with breast cancer. *Med Sci Sports Exerc* 2021; **53:** 496–504.

12 Ligibel JA, Bohlke K, May AM, et al. Exercise, diet, and weight management during cancer treatment: ASCO Guideline. *J Clin Oncol* 2022; **40:** 2491–507.

13 Rock CL, Thomson CA, Sullivan KR, et al. American Cancer Society nutrition and physical activity guideline for cancer survivors. *CA Cancer J Clin* 2022; **72:** 230–62.

14 Pegram M, Jackisch C, Johnston SRD. Estrogen/HER2 receptor crosstalk in breast cancer: combination therapies to improve outcomes for patients with hormone receptor-positive/HER2-positive breast cancer. *NPJ Breast Cancer* 2023; **9:** 45.

15 Tommasi C, Airò G, Pratticò F, et al. Hormone receptor-positive/HER2-positive breast cancer: hormone therapy and anti-HER2 treatment: an update on treatment strategies. *J Clin Med* 2024; **13:** 1873.

16 Fox S, Speirs V, Shaaban AM. Male breast cancer: an update. *Virchows Arch* 2022; **480:** 85–93.

17 Li Y, Guo Y, Chen F, Cui Y, Chen X, Shi G. Male breast cancer differs from female breast cancer in molecular features that affect prognoses and drug responses. *Transl Oncol* 2024; **45:** 101980.

18 Xuan L, Bai C, Ju Z, et al. Radiation-targeted immunotherapy: a new perspective in cancer radiotherapy. *Cytokine Growth Factor Rev* 2024; **75:** 1–11.

19 Livshits Z, Rao RB, Smith SW. An approach to chemotherapy-associated toxicity. *Emerg Med Clin North Am* 2014; **32:** 167–203.

20 Zeien J, Qiu W, Triay M, et al. Clinical implications of chemotherapeutic agent organ toxicity on perioperative care. *Biomed Pharmacother* 2022; **146:** 112503.

21 Crawford J, Dale DC, Lyman GH. Chemotherapy-induced neutropenia: risks, consequences, and new directions for its management. *Cancer* 2004; **100:** 228–37.

22 Courneya KS, Segal RJ, Mackey JR, et al. Effects of aerobic and resistance exercise in breast cancer patients receiving adjuvant chemotherapy: a multicenter randomized controlled trial. *J Clin Oncol* 2007; **25:** 4396–404.

23 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.

24 Hiensch AE, Depenbusch J, Schmidt ME, et al. Supervised, structured and individualized exercise in metastatic breast cancer: a randomized controlled trial. *Nat Med* 2024; **30:** 2957–66.

25 Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2021. *CA Cancer J Clin* 2021; **71:** 7–33.

26 Sasso JP, Eves ND, Christensen JF, Koelwyn GJ, Scott J, Jones LW. A framework for prescription in exercise-oncology research. *J Cachexia Sarcopenia Muscle* 2015; **6:** 115–24.

27 Bland KA, Kirkham AA, Bovard J, et al. Effect of exercise on taxane chemotherapy-induced peripheral neuropathy in women with breast cancer: a randomized controlled trial. *Clin Breast Cancer* 2019; **19:** 411–22.

28 Kearney N, Connolly D, Begic S, Mockler D, Guinan E. Feasibility metrics of exercise interventions during chemotherapy: a systematic review. *Crit Rev Oncol Hematol* 2024; **195:** 104272.

29 Walker RC, Pezeshki P, Barman S, et al. Exercise during chemotherapy for cancer: a systematic review. *J Surg Oncol* 2024; **130:** 1725–36.

30 Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; **372:** n71.

31 Cochrane handbook for systematic reviews of interventions. In: Higgins JPT, Thomas J, Chandler J, et al, eds. 2024. www.cochrane.org/handbook (accessed Nov 16, 2025).

32 Howard BE, Phillips J, Miller K, et al. SWIFT-Review: a text-mining workbench for systematic review. *Syst Rev* 2016; **5:** 87.

33 Brydges CR. Effect size guidelines, sample size calculations, and statistical power in gerontology. *Innov Aging* 2019; **3:** igz036.

34 Hedges LV. Interpretation of the standardized mean difference effect size when distributions are not normal or homoscedastic. *Educ Psychol Meas* 2024; **85:** 245–57.

35 Viechtbauer W. Conducting meta-analyses in R with the metafor package. *J Stat Softw* 2010; **36:** 1–48.

36 Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366:** l4898.

37 Cheung MWL. Modeling dependent effect sizes with three-level meta-analyses: a structural equation modeling approach. *Psychol Methods* 2014; **19:** 211–29.

38 Park S, Beretvas SN. Synthesizing effects for multiple outcomes per study using robust variance estimation versus the three-level model. *Behav Res Methods* 2019; **51:** 152–71.

39 Van Den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J. Three-level meta-analysis of dependent effect sizes. *Behav Res Methods* 2013; **45:** 576–94.

40 Pustejovsky JE, Tipton E. Meta-analysis with robust variance estimation: expanding the range of working models. *Prev Sci* 2022; **23:** 425–38.

41 Gokal K, Wallis D, Ahmed S, Boiangiu I, Kancherla K, Munir F. Effects of a self-managed home-based walking intervention on psychosocial health outcomes for breast cancer patients receiving chemotherapy: a randomised controlled trial. *Support Care Cancer* 2016; **24:** 1139–66.

42 van Waart H, Stuiver MM, van Harten WH, et al. Effect of low-intensity physical activity and moderate- to high-intensity physical exercise during adjuvant chemotherapy on physical fitness, fatigue, and chemotherapy completion rates: results of the PACES randomized clinical trial. *J Clin Oncol* 2015; **33:** 1918–27.

43 Sturgeon K, Smith A, Federici E, et al. Feasibility of a tailored home-based exercise intervention during neoadjuvant chemotherapy in breast cancer patients. *BMC Sports Sci Med Rehabil* 2022; **14:** 31.

44 Al-Majid S, Wilson LD, Rakovski C, Coburn JW. Effects of exercise on biobehavioral outcomes of fatigue during cancer treatment: results of a feasibility study. *Biol Res Nurs* 2015; **17:** 40–48.

45 Darvishi E, Musarezaie A, Bahrami M, Karimian J. The effect of a combined exercise program on the fatigue severity of patients with breast cancer undergoing chemotherapy: a randomized clinical trial study. *Iran J Nurs Midwifery Res* 2023; **28:** 398–404.

46 Lee K, Norris MK, Wang E, Dieli-Conwright CM. Effect of high-intensity interval training on patient-reported outcomes and physical function in women with breast cancer receiving anthracycline-based chemotherapy. *Support Care Cancer* 2021; **29:** 6863–70.

47 Yang CY, Tsai JC, Huang YC, Lin CC. Effects of a home-based walking program on perceived symptom and mood status in postoperative breast cancer women receiving adjuvant chemotherapy. *J Adv Nurs* 2011; **67:** 158–68.

48 Maryam A, Fazlollah A, Eesa M, Ebrahim H, Abbas VF. The effect of designed exercise programme on quality of life in women with breast cancer receiving chemotherapy. *Scand J Caring Sci* 2010; **24:** 251–58.

49 He X, Ng MSN, Choi KC, So WKW. Effects of a 16-week dance intervention on the symptom cluster of fatigue–sleep disturbance–depression and quality of life among patients with breast cancer undergoing adjuvant chemotherapy: a randomized controlled trial. *Int J Nurs Stud* 2022; **133:** 104317.

50 Li H, Sang D, Gong L, et al. Improving physical and mental health in women with breast cancer undergoing anthracycline-based chemotherapy through wearable device-based aerobic exercise: a randomized controlled trial. *Front Public Health* 2024; **12:** 1451101.

51 Moros MT, Ruidiaz M, Caballero A, Serrano E, Martinez V, Tres A. Effects of an exercise training program on the quality of life of women with breast cancer on chemotherapy. *Rev Med Chil* 2010; **138:** 715–22.

52 Antunes P, Joaquim A, Sampaio F, et al. Exercise training benefits health-related quality of life and functional capacity during breast cancer chemotherapy: a randomized controlled trial. *Med Sci Sports Exerc* 2024; **56:** 600–11.

53 Cornette T, Vincent F, Mandigout S, et al. Effects of home-based exercise training on VO2 in breast cancer patients under adjuvant or neoadjuvant chemotherapy (SAPA): a randomized controlled trial. *Eur J Phys Rehabil Med* 2016; **52:** 223–32.

54 Husebø AML, Dyrstad SM, Mjaaland I, et al. Effects of scheduled exercise on cancer-related fatigue in women with early breast cancer. *ScientificWorldJournal* 2014; **2014:** 271828.

55 Scott JM, Thomas SM, Peppercorn JM, et al. Effects of exercise therapy dosing schedule on impaired cardiorespiratory fitness in patients with primary breast cancer: a randomized controlled trial. *Circulation* 2020; **141:** 560–70.

56 Naraphong W, Lane A, Schafer J, Whitmer K, Wilson BRA. Exercise intervention for fatigue-related symptoms in Thai women with breast cancer: a pilot study. *Nurs Health Sci* 2015; **17:** 33–41.

57 Suárez-Alcázar M, García-Roca M, Collado-Boira E, et al. Exercise and quality of life (QoL) in patients undergoing active breast cancer treatment-comparison of three modalities of a 24-week exercise program-a randomized clinical trial. *Healthcare (Basel)* 2024; **12:** 1107.

58 Brunet J, Sharma S, Zadravec K, et al. Aerobic exercise and CogniTIVe functioning in women with breAsT cancEr (ACTIVATE): a randomized controlled trial. *Cancer* 2025; **131:** e35540.

59 Klavina A, Ceseiko R, Campa M, et al. The effect of high-intensity interval training on quality of life and incidence of chemotherapy side effects in women with breast cancer. *Integr Cancer Ther* 2024; **23:** 15347354241297385.

60 Chung WP, Yang HL, Hsu YT, et al. Real-time exercise reduces impaired cardiac function in breast cancer patients undergoing chemotherapy: a randomized controlled trial. *Ann Phys Rehabil Med* 2022; **65:** 101485.

61 Lahart IM, Metsios GS, Nevill AM, Carmichael AR. Physical activity, risk of death and recurrence in breast cancer survivors: a systematic review and meta-analysis of epidemiological studies. *Acta Oncol* 2015; **54:** 635–54.

62 Spence RR, Heesch KC, Brown WJ. Exercise and cancer rehabilitation: a systematic review. *Cancer Treat Rev* 2010; **36:** 185–94.

63 Albini A, La Vecchia C, Magnoni F, et al. Physical activity and exercise health benefits: cancer prevention, interception, and survival. *Eur J Cancer Prev* 2025; **34:** 24–39.

64 Orlandella FM, De Stefano AE, Iervolino PLC, Buono P, Soricelli A, Salvatore G. Dissecting the molecular pathways involved in the effects of physical activity on breast cancers cells: a narrative review. *Life Sci* 2021; **265:** 118790.

65 Schmidt S, Monk JM, Robinson LE, Mourtzakis M. The integrative role of leptin, oestrogen and the insulin family in obesity-associated breast cancer: potential effects of exercise. *Obes Rev* 2015; **16:** 473–87.

66 Ligibel JA, Bohlke K, May AM, et al. Exercise, diet, and weight management during cancer treatment: ASCO Guideline. *J Clin Oncol* 2022; **40:** 2491–507.

67 Slade SC, Dionne CE, Underwood M, Buchbinder R. Consensus on Exercise Reporting Template (CERT): explanation and elaboration statement. *Br J Sports Med* 2016; **50:** 1428–37.

68 Subialka JA, McConnell RC, Vosburgh E, et al. Using the Consensus on Exercise Reporting Template (CERT) checklist at the exercise level to assess the completeness of exercise reporting: a methodological review. *JOSPT Methods* 2025; **1:** 102–12.