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Comparative Efficacy of Different Exercise Modalities for Cancer-Related Fatigue, Anxiety and Depression Symptoms, and Health-Related Quality of Life in Cancer Survivors: A Systematic Review and Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 November 2025 and was last updated on 27 November 2025.

INTRODUCTION

Review question / Objective This systematic review and network meta-analysis aims to determine the comparative efficacy of different exercise training modalities for improving cancer-related fatigue, anxiety and depression symptoms, and health-related quality of life in adult cancer survivors. The review seeks to address the following research questions.

Rationale Cancer survivorship continues to grow globally, with over 18 million cancer survivors worldwide experiencing persistent treatment-related symptoms that significantly impact quality of life. Cancer-related fatigue affects 80-90% of cancer survivors and is consistently rated as the most distressing symptom, often persisting years after treatment completion. Additionally, anxiety and depression prevalence in cancer survivors (20-30%) is nearly double that of the general population, contributing to decreased quality of life and functional capacity. Exercise therapy has emerged as a cornerstone intervention for managing cancer survivorship symptoms, with major professional organizations including the American College of Sports Medicine (ACSM), American Cancer Society, and Clinical Oncology Society of Australia endorsing exercise as standard care. Current evidence demonstrates that exercise interventions significantly improve cancer-related fatigue (moderate effect sizes, SMD = 0.27-0.46), quality of life measures.

Condition being studied This review will systematically evaluate the comparative effects of different exercise training modalities on cancer-related fatigue, anxiety and depression symptoms, health-related quality of life, and physical functioning in adult cancer survivors. Cancer survivors are defined as individuals who have completed primary cancer treatment (surgery, chemotherapy, radiotherapy) and are at least 3

months post-treatment completion, excluding those receiving active palliative care.

METHODS

Participant or population 12.Participants or Population
12.1.Inclusion Criteria:
1.Adult cancer survivors (≥18 years) who have completed primary cancer treatment
2.Minimum 3 months post-completion of active treatment (surgery, chemotherapy, radiotherapy)
3.Any cancer type (solid tumors or hematological malignancies)
4.Any cancer stage at diagnosis (early to advanced)
5.Any treatment history combination
6.Studies conducted in any setting (hospital, community, home-based)
12.2.Exclusion Criteria:
1.Patients currently receiving active cancer treatment (excluding maintenance therapy)
2.Studies exclusively including patients in active palliative care
3.Pediatric populations (<18 years)
4.Studies with mixed populations where <80% are cancer survivors
5.Studies without clear documentation of cancer survivor status.

Intervention The interventions of interest are structured exercise training programs delivered to cancer survivors, classified into five primary categories:
1.Aerobic Exercise (AE): Continuous rhythmic activities engaging large muscle groups; Examples: walking, cycling, swimming, elliptical training, dancing; Minimum duration: 4 weeks, ≥2 sessions per week
2.Resistance Training (RT): Progressive resistance exercises using weights, machines, elastic bands, or bodyweight; Targeting major muscle groups with systematic overload progression; Minimum duration: 4 weeks, ≥2 sessions per week
3.Combined Aerobic-Resistance Training (CART): Programs incorporating both aerobic and resistance components; May be concurrent within sessions or alternating between sessions; Minimum duration: 4 weeks
4.Mind-Body Exercises (MBE): Yoga (all styles including Hatha, Iyengar, restorative, vinyasa); Tai Chi and Qigong practices; Meditation-based movement practices; Minimum duration: 4 weeks
Mixed/Other Exercise: Programs combining elements not fitting above categories or unique approaches; Balance training, Pilates, functional training programs;
Minimum Intervention Requirements: Total intervention duration ≥4 weeks; Documented exercise prescription parameters (frequency, intensity, and/or duration); Clear description of exercise components and delivery method.

Comparator
14.Comparator
Eligible Comparator Groups:
1.Usual care/standard care: Standard medical follow-up without structured exercise
2.Wait-list control groups: Delayed intervention controls
3.Attention control: Non-exercise interventions with similar contact time (education, counseling)
Other exercise modalities: For direct exercise-to-exercise comparisons, the comparator requirements include: Same population characteristics as intervention group; Same outcome measurement timepoints; Clearly documented control intervention description; Studies without appropriate control groups will be excluded.

Study designs to be included 1.Included Study Designs: Randomized controlled trials (individual or cluster randomization); Parallel-group design (primary) or crossover design with adequate washout; Single-blind, double-blind, or open-label trials; Single-center or multi-center studies2.Minimum Study Requirements: Intervention duration ≥4 weeks; Minimum sample size: 20 participants per arm (40 total); Adequate randomization procedures described; Appropriate control group as defined above; At least one primary outcome measure reported.

Eligibility criteria
16.1.Inclusion Criteria:
1.Study Design: Randomized controlled trials (parallel or crossover with adequate washout)
2.Population: Adult cancer survivors (≥18 years) ≥3 months post-treatment
3.Intervention: Structured exercise training program ≥4 weeks duration
4.Comparator: Usual care, wait-list, attention control, or other exercise modality
5.Outcomes: At least one primary outcome (cancer-related fatigue or health-related quality of life)
6.Duration: Intervention period ≥4 weeks with post-intervention assessment
7.Language: Published in English
8.Publication Date: January 2010 to present
9.Publication Type: Peer-reviewed journal articles and clinical trial reports
10.Data Availability: Sufficient data for effect size calculation

16.2.Exclusion Criteria:
1.Study Design: Non-randomized studies, observational studies, case reports, reviews, conference abstracts
2.Population: Patients receiving active treatment, palliative care populations, pediatric patients
3.Intervention: Single-session studies, interventions <4 weeks, non-exercise interventions
4.Comparator: No appropriate control group, active treatment controls
5.Outcomes: Studies not reporting any outcomes of interest
6.Data: Insufficient data for analysis, duplicate publications.

Information sources This systematic review will adhere to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Network Meta-Analysis (PRISMA-NMA) extension guidelines. Comprehensive searches will be conducted across five major databases as detailed in the search strategy section. Reference management and screening: Reference Management: Zotero for bibliography organization and export. Screening Platform: EPPI-Reviewer 4 for systematic screening and duplicate removal. Review Team: Minimum 2 independent reviewers with senior reviewer conflict resolution.

Main outcome(s)
18.1.Primary Outcomes:
1.Cancer-Related Fatigue - Measurement Hierarchy: Preferred: Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue); Acceptable: Piper Fatigue Scale, Multidimensional Fatigue Inventory (MFI-20), Brief Fatigue Inventory, EORTC QLQ-C30 Fatigue subscale ; Timing: Post-intervention assessment (immediately following intervention completion); Clinically Important Difference: 3-point change on FACIT-Fatigue scale
2.Health-Related Quality of Life - Global Score - Measurement Hierarchy: Preferred: EORTC QLQ-C30 Global Health Status scale; Acceptable: FACT-General (FACT-G), SF-36 Physical/Mental Component Summary, EORTC QLQ-C30 Summary Score; Timing: Post-intervention assessment; Clinically Important Difference: 10-point change on EORTC QLQ-C30 (0-100 scale).

Additional outcome(s) 19.1.Secondary Outcomes:
1.Anxiety and Depression - Measurement Hierarchy: Preferred: Hospital Anxiety and Depression Scale (HADS) total score or subscales; Acceptable: Beck Depression Inventory, Center for Epidemiologic Studies Depression Scale, Patient Health Questionnaire-9, Generalized Anxiety Disorder-7; Clinically Important Difference: 1.5-point change on HADS
2.Physical Functioning - Measurement Hierarchy: Preferred: EORTC QLQ-C30 Physical Functioning subscale; Acceptable: FACT Physical Well-Being, SF-36 Physical Functioning, objective measures (6-minute walk test, VO2peak).

Data management
20.1.Study Selection Process:
Two independent reviewers will conduct study selection in two phases using EPPI-Reviewer 4:
1.Title and Abstract Screening: Initial screening based on inclusion/exclusion criteria
2.Full-Text Review: Detailed evaluation of potentially eligible studies
3.Conflict Resolution:
Discussion between primary reviewers for initial conflict resolution
Senior reviewer consultation for unresolved disagreements
Team discussion for complex methodological decisions
4.Data Extraction:
Standardized extraction forms developed and pilot-tested
Two reviewers independently extract data from included studies
Excel templates for systematic data collection
Regular data backup and version control with audit trail
5.Reference and Data Management:
Zotero: Reference management and organization
EPPI-Reviewer 4: Screening workflow and duplicate removal
Data Storage: Secure cloud-based storage with regular backups.

Quality assessment / Risk of bias analysis
21.1.Assessment Tools:
Revised Cochrane Risk of Bias Tool (RoB 2.0) for randomized controlled trials
GRADE approach for overall evidence quality assessment across the network
21.2.Risk of Bias Domains:
1.Randomization Process: Sequence generation and allocation concealment
2.Deviations from Intended Interventions: Blinding and adherence assessment
3.Missing Outcome Data: Completeness and handling methods
4.Measurement of Outcomes: Outcome assessor blinding when feasible
5.Selection of Reported Results: Selective reporting bias assessment
21.3.Network-Specific Quality Assessment:

Transitivity Assessment: Comparison of study and population characteristics across treatment comparisons
Consistency Evaluation: Local and global inconsistency testing
Publication Bias: Comparison-adjusted funnel plots and statistical testing.

Strategy of data synthesis
22.1.Network Meta-Analysis Approach:
Primary Analysis Platform: MetaInsight (University of Bristol) for Bayesian network meta-analysis
Model: Random-effects inconsistency model as primary analysis
Effect Measure: Standardized mean difference (SMD) with 95% credible intervals
MCMC Settings: 50,000 iterations, 20,000 burn-in, thinning every 10th iteration
Secondary Analysis Tools:
R Software: netmeta package for complex meta-regression and sensitivity analyses
RevMan 5.4: Traditional pairwise meta-analysis for subgroup analyses and forest plots
Analysis Strategy:
1.Network Geometry: Assessment of treatment network connectivity and visualization
2.Statistical Model: Random-effects model accounting for between-study heterogeneity
3.Treatment Rankings: Surface Under the Cumulative Ranking Curve (SUCRA) probabilities
4.Consistency Assessment: Node-splitting approach and inconsistency modeling
6.Effect Size Calculation:
Standardized Mean Difference: Using Hedges' g for continuous.

Subgroup analysis
Pre-planned Subgroup Analyses:
1.Cancer Type: Breast cancer vs. other solid tumors vs. hematological cancers
2.Time Since Treatment: 8 weeks
5.Study Quality: Low vs. moderate/high risk of bias studies
Meta-Regression Analyses:
Continuous Moderators: Age, baseline symptom severity, intervention duration
Exercise Parameters: Total exercise volume, session frequency, intervention intensity
Subgroup Analysis Methods:
RevMan 5.4: Traditional subgroup meta-analysis with forest plots
R Software: Network meta-regression for complex moderator analyses
MetaInsight: Subgroup-specific networks when sample size permits
7.Sensitivity Analysis.

Sensitivity analysis 1.Study Quality: Excluding studies with high overall risk of bias
2.Sample Size: Excluding studies with <50 participants per arm
3.Population Homogeneity: Excluding studies with mixed cancer populations
4.Intervention Fidelity: Including only studies with clearly defined exercise protocols
5.Statistical Model: Fixed-effects vs. random-effects model comparison
6.Outcome Measures: Restricting to preferred outcome instruments only
8.Publication Bias Assessment:
Comparison-Adjusted Funnel Plots: Visual assessment of small study effects
Egger's Test: Statistical testing for funnel plot asymmetry
Sensitivity Analysis: Impact of excluding small studies on network estimates.

Language restriction Only studies published in English will be included in this systematic review and network meta-analysis due to resource constraints and translation limitations.

Country(ies) involved China.

Keywords Exercise; cancer survivors; cancer survivorship; fatigue; quality of life; anxiety; depression; network meta-analysis; systematic review; aerobic exercise; resistance training; yoga.

Dissemination plans Exercise; cancer survivors; cancer survivorship; fatigue; quality of life; anxiety; depression; network meta-analysis; systematic review; aerobic exercise; resistance training; yoga; tai chi; oncology; rehabilitation.

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