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INPLASY

Comparative Efficacy and Dose-Response of Exercise Modalities for Cancer-Related Fatigue: A Systematic Review and Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - No funding available at the moment.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025120050

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 December 2025 and was last updated on 14 December 2025.

INTRODUCTION

Review question / Objective Eligibility was mapped to the PRISMA-PICOS framework: (P) histologically confirmed malignancy, any stage or treatment phase; (I) supervised exercise protocols (aerobic, resistance, mind-body, or multimodal); (C) alternative exercise regimens, usual care, or no-exercise control; (O) CRF severity captured by validated patient-reported outcomes—FACIT-F, PFS, MFI, or BFI; (S) randomized controlled trials exclusively; quasi-experimental and other non-randomized designs were discarded.Cancer-related fatigue (CRF) dominates the symptom experience of active oncology patients and frequently persists into survivorship. Operationally, it is defined as a distressing, sustained sensation of whole-body exhaustion that is refractory to rest and disproportionate to preceding exertion. Prospective surveys report point-prevalences of 70–100 % during cytotoxic or targeted therapy, while 20–30 % of post-treatment survivors remain symptomatic for years. The mechanistic substrate is multifactorial, encompassing systemic inflammation, skeletal-myocyte bioenergetic reprogramming, and treatment-induced anemia. No single pharmacologic agent has demonstrated consistent efficacy against this network pathophysiology, propelling exercise-based, non-pharmacologic interventions to the forefront of supportive-oncology research.Inclusion criteria for this study are based on the PICOS principle recommended by PRISMA: Population (P): Cancer patients diagnosed pathologically, regardless of cancer type, stage, or treatment phase. Intervention (I): Structured exercise interventions, including but not limited to aerobic exercise, resistance training, mind-body exercise, or multimodal exercise programs. Comparison (C): Other types of exercise interventions, usual care, or no intervention control groups. Outcome (O): The primary outcome is the severity of cancer-related fatigue, assessed using validated self-report scales such as the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), Piper Fatigue Scale (PFS), Multidimensional Fatigue Inventory (MFI), or Brief Fatigue Inventory (BFI). Study design (S):

Randomized controlled trials (RCTs). Non-randomized studies, quasi-experimental studies, and other non-RCTs will be excluded.

Condition being studied Cancer-related fatigue (CRF) dominates the symptom experience of active oncology patients and frequently persists into survivorship. Operationally, it is defined as a distressing, sustained sensation of whole-body exhaustion that is refractory to rest and disproportionate to preceding exertion. Prospective surveys report point-prevalences of 70–100 % during cytotoxic or targeted therapy, while 20–30 % of post-treatment survivors remain symptomatic for years. The mechanistic substrate is multifactorial, encompassing systemic inflammation, skeletal-myocyte bioenergetic reprogramming, and treatment-induced anemia. No single pharmacologic agent has demonstrated consistent efficacy against this network pathophysiology, propelling exercise-based, non-pharmacologic interventions to the forefront of supportive-oncology research.Cancer-Related Fatigue (CRF) is one of the most common and debilitating side effects experienced by patients during cancer and its treatment. Clinically, CRF is characterized by a persistent, subjective sense of exhaustion that is disproportionate to recent activity levels and cannot be alleviated by rest. Epidemiological data indicate that the incidence of CRF among cancer patients undergoing active treatment can range from 70% to 100%. Furthermore, approximately 20% to 30% of cancer survivors continue to experience long-term CRF years after treatment completion, highlighting it as a significant long-term survivorship issue. The pathophysiology of CRF is highly complex, potentially involving elevated levels of inflammatory cytokines, altered muscle metabolism, and anemia, among other factors. Due to this complexity, effective monotherapy pharmacological treatments for CRF are lacking in clinical practice. Consequently, developing effective non-pharmacological strategies, particularly exercise-based interventions, has become an urgent priority in oncology supportive care.

METHODS

Participant or population Histologically verified malignancy, irrespective of subtype, stage, or treatment timeline.

Intervention Supervised, protocolized exercise (aerobic, resistance, mind-body, or any synergistic combination thereof).

Comparator Comparator: alternative exercise regimens, usual oncologic care, or non-exercise control.

Study designs to be included Randomized controlled trials exclusively; quasi-experimental or observational designs were disqualified. Randomized Controlled Trial.

Eligibility criteria Eligibility followed the PRISMA-PICOS schema; any design lacking random allocation (quasi-experimental, single-arm, or observational) was ineligible.
Exclusions: (i) duplicate or off-topic citations; (ii) reviews, case reports, consensus statements, conference abstracts; (iii) non-human data; (iv) non-randomized comparators; (v) trials permitting concomitant pharmacologic or behavioral co-interventions that could obscure exercise-specific effects; (vi) manuscripts whose full text or raw data were inaccessible.

Information sources A systematic search of PubMed, Embase, and the Web of Science Core Collection will be conducted for records indexed from database inception through 1 August 2025.

Main outcome(s) CRF intensity quantified by validated patient-reported outcome measures—FACIT-F, PFS, MFI, or BFI.

Quality assessment / Risk of bias analysis Confidence in the network estimates will be appraised with CINeMA, which grades within-study risk , reporting bias, indirectness, heterogeneity, incoherence, and imprecision. Each domain is integrated into an overall rating of high, moderate, low, or very low confidence. Two reviewers will score independently; discrepancies reconciled by consensus or adjudication of a third.

Strategy of data synthesis Using Stata 15.1, random-effects NMA estimated MD/SMD (95% CI). Network plots, χ^2 and node-split tests assessed inconsistency; SUCRA (10 000 MCMC) ranked treatments. Bias was checked with comparison-adjusted funnel plots.

Subgroup analysis Between-subgroup heterogeneity remains to be delineated as a potential source of refined inference. The present estimation was restricted to the aggregate cohort; expansion to a larger population sample is prerequisite for stratified modelling intended to inform precision-oriented decision algorithms.

Sensitivity analysis Sensitivity analysis, regarded as a critical validity checkpoint, was deferred until

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the core model reaches full stabilization. Once the analytical framework is frozen, perturbation of each fatigue dimension will be quantified to delineate the contribution of dominant uncertainty sources to the endpoint variance, thereby furnishing an evidence base for subsequent risk-mitigation strategies.

Country(ies) involved China.

Keywords Cancer-Related Fatigue; Exercise Therapy; Network Meta-Analysis; Dose-Response Relationship; Clinical symptom.

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