

Review

Comparative effects of different exercise interventions on the mental health of cancer patients: A systematic review and network meta-analysis

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Abstract: Background: Exercise is recognized as an effective non-pharmacological intervention to improve psychological outcomes in cancer patients, but comparative evidence across exercise types remains unclear. **Methods:** A systematic review and network meta-analysis of 40 randomized controlled trials involving 4082 cancer patients was conducted to compare exercise modalities on quality of life and fatigue. Standardized mean differences (SMDs) and 95% confidence intervals (CIs) were calculated, and moderation analyses examined intervention duration and personalization. **Results:** High-intensity interval training (HIIT) showed the greatest psychological benefits, producing the largest fatigue reduction (SMD = 0.78, 95% CI: 0.52–1.04). Interventions lasting 16–24 weeks demonstrated optimal overall effects. Higher levels of supervision significantly enhanced outcomes, with personalized programs outperforming low-personalization approaches. **Conclusion:** HIIT and personalized, adequately long exercise programs provide the most effective psychological improvements for cancer patients. These findings support the integration of structured and individualized exercise prescriptions into routine cancer care.

Keywords: cancer; exercise intervention; high-intensity interval training; mental health; network meta-analysis; quality of life

1. Introduction

Cancer and its treatments impose a substantial burden on patients' physical and mental well-being, particularly in the domain of psychological health. Cancer patients demonstrate a two-to-three fold increased prevalence of depression and anxiety relative to the general population, significantly affecting their quality of life and treatment outcomes [1]. Following diagnosis, approximately 40–50% of patients develop clinically significant psychological distress, including fear of death, psychological adaptation to physical changes, and stress from altered social roles [2]. This pattern persists across various cancer types, especially when patients simultaneously undergo active treatments such as chemotherapy, radiotherapy, or surgery.

Exercise interventions have demonstrated efficacy in ameliorating psychological distress and enhancing quality of life among cancer populations. Over recent decades, scientific evidence has demonstrated that physical activity can alleviate cancer-related fatigue, enhance psychological resilience, and reduce symptoms of depression and anxiety [3]. Multiple clinical trials have verified that cancer patients

participating in structured exercise programs report a higher quality of life and lower levels of psychological distress [4]. These positive effects may derive from exercise's regulatory impact on the neuroendocrine system, increased social interaction, and restoration of a sense of bodily control.

Cancer patients can choose from diverse exercise intervention types, including aerobic training, resistance training, high-intensity interval training (HIIT), and comprehensive programs. Aerobic exercises such as walking and cycling have been extensively applied across various cancers, demonstrating benefits for psychological health [5]. Resistance training enhances self-confidence and independence by improving muscle strength and physical function [6]. High-intensity interval training, as a time-efficient alternative, has garnered increasing attention in recent years [7]. Additionally, integrated intervention programs combining multiple approaches may offer more comprehensive benefits [8].

Despite existing research confirming the overall effectiveness of exercise interventions, controversy persists regarding which type of exercise is most effective for specific patient populations. Most previous studies typically focus on comparing single interventions with control groups, with few studies directly comparing different types of exercise interventions [9]. Furthermore, clear guidelines for optimal exercise prescriptions for specific cancer types and treatment stages remain lacking [10]. In this context, network meta-analysis provides a powerful methodological framework capable of simultaneously comparing multiple intervention strategies, even when these interventions were not directly compared in original studies.

This research aims to systematically evaluate and compare the effects of different types of exercise interventions on cancer patients' psychological health through network meta-analysis. The study will explore the relative effectiveness of various exercise forms in improving quality of life, alleviating fatigue, and relieving anxiety and depression. The anticipated results will provide an empirical foundation for developing individualized exercise prescriptions in clinical practice, thereby optimizing psychological health outcomes for cancer survivors [11].

2. Methods

2.1. Search strategy

A comprehensive literature search was conducted using multiple databases, including PubMed, Embase, Web of Science, Cochrane Library, CINAHL, and PsycINFO, from inception through April 2024. Search strategies combined MeSH terms and free-text keywords related to cancer, exercise interventions, and psychological outcomes. The complete search strategy implemented in PubMed combined Medical Subject Headings (MeSH) and free-text terms as follows: (((“Neoplasms”[MeSH] OR cancer*[tiab] OR neoplas*[tiab] OR tumor*[tiab] OR tumour*[tiab] OR malignan*[tiab] OR carcinoma*[tiab] OR oncolog*[tiab]) AND (“Exercise”[MeSH] OR “Exercise Therapy”[MeSH] OR “Resistance Training”[MeSH] OR “High-Intensity Interval Training”[MeSH] OR “Yoga”[MeSH] OR “Tai Ji”[MeSH] OR exercis*[tiab] OR “physical activit*”[tiab] OR aerobic*[-

tiab] OR “resistance train*”[tiab] OR “strength train*”[tiab] OR “interval training”[tiab] OR HIIT[tiab] OR yoga[tiab] OR “tai chi”[tiab] OR “mind-body”[tiab]) AND (“Quality of Life”[MeSH] OR “Anxiety”[MeSH] OR “Depression”[MeSH] OR “Fatigue”[MeSH] OR “Mental Health”[MeSH] OR “quality of life”[tiab] OR QoL[tiab] OR anxiety[tiab] OR depression[tiab] OR fatigue[tiab] OR “psychological wellbeing”[tiab] OR “mental health”[tiab] OR “psychological distress”[tiab] OR mood[tiab] OR “emotional well-being”[tiab])) AND (“Randomized Controlled Trial”[pt] OR “Controlled Clinical Trial”[pt] OR randomized[tiab] OR randomised[tiab] OR RCT[tiab]) NOT (“Animals”[MeSH] NOT “Humans”[MeSH])). This strategy was adapted for other databases according to their specific syntax and controlled vocabulary requirements.

Study selection followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Network Meta-Analyses (PRISMA-NMA) guidelines [9]. All potentially relevant studies were independently screened by two reviewers at title/abstract level and subsequently at the full-text level against pre-defined inclusion criteria. The inclusion criteria specified randomized controlled trials (RCTs) examining exercise interventions in cancer patients with psychological health outcomes. Studies were excluded if they involved non-exercise interventions, non-cancer populations, or lacked relevant psychological outcome measures [12]. Disagreements between reviewers were resolved through discussion with a third reviewer until consensus was reached. The literature screening process identified 95 potentially eligible studies, with 40 studies ultimately meeting all inclusion criteria for the network meta-analysis [13,14].

2.2. Inclusion and exclusion criteria

The present network meta-analysis incorporated randomized controlled trials (RCTs) exclusively, as this design provides the highest level of evidence for intervention efficacy by minimizing selection bias and controlling for confounding factors [15]. Studies were eligible if they examined adult cancer patients (≥ 18 years) with a histologically confirmed diagnosis of any cancer type at any disease stage, either during active treatment or in survivorship. No restrictions were placed on cancer type to enable comprehensive analysis across malignancies, though subgroup analyses were planned for major cancer categories including breast, colorectal, prostate, and lung cancer. Intervention eligibility encompassed structured exercise programs including aerobic training (e.g., walking, cycling); resistance training (e.g., weight-bearing exercises); HIIT; mixed-modality training; and mind–body exercise approaches such as yoga or tai chi, with clear descriptions of frequency, intensity, duration, and supervision level [16].

Exercise interventions were classified according to established taxonomic criteria based on the primary physiological systems engaged and training principles employed. Aerobic exercise was defined as continuous rhythmic activities utilizing large muscle groups at 40–85% of heart rate reserve or 50–85% of maximum oxygen uptake (VO_{2max}) for a minimum duration of 20 min per session, including activities such as walking, cycling, swimming, or jogging. Resistance training was

characterized by exercises involving skeletal muscle contraction against external resistance with progressive overload principles, typically performed at 40–80% of one-repetition maximum (1RM) or using resistance bands with comparable perceived exertion levels, encompassing free weights, machine-based exercises, or bodyweight training. HIIT was identified by alternating periods of vigorous exercise ($\geq 85\%$ maximum heart rate or ≥ 6 on the Borg CR-10 scale) with recovery intervals, maintaining work-to-rest ratios between 1:1 and 1:4. Combined or mixed-modality training incorporated elements from at least two distinct exercise categories within the same intervention program, with each component constituting a minimum of 25% of total exercise time. Mind–body exercises were distinguished by their integration of physical movement with mental focus and controlled breathing techniques, including practices such as yoga, tai chi, qigong, or Pilates, characterized by emphasis on postural alignment, flexibility, and meditative components. When studies employed exercise interventions that could potentially fit multiple categories, classification was determined by the predominant training modality accounting for $>50\%$ of the intervention content, with secondary modalities noted in the data extraction process. Studies providing insufficient detail for definitive categorization were classified based on the predominant exercise characteristics described, with uncertainty noted in the quality assessment. Three studies (7.5%) presented intervention descriptions that precluded clear classification into a single category and were, therefore, analyzed separately in sensitivity analyses to assess their impact on the overall network estimates.

Control conditions included usual care, wait-list controls, or attention controls. The primary outcome measures encompassed validated assessments of psychological health domains: health-related quality of life measured by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) or SF-36 (36-Item Short Form Health Survey); cancer-related fatigue assessed by FACIT-Fatigue or similar scales; and anxiety and depression measured by Hospital Anxiety and Depression Scale (HADS) or comparable instruments [17,18]. Studies were excluded if they involved non-exercise interventions, combined exercise with other therapeutic modalities without separate group analysis, or lacked baseline and follow-up psychological outcome data.

2.3. Data extraction

A standardized data extraction form was developed to systematically collect information from eligible studies. Two independent reviewers extracted data from each included study, with any discrepancies resolved through discussion and consultation with a third reviewer when necessary. Study characteristics extracted included bibliographic details (authors, publication year, journal); methodological attributes (study design, randomization method, blinding procedures); sample characteristics (sample size, age, gender distribution, cancer type and stage, treatment status); and follow-up duration [19]. Detailed information regarding exercise interventions was recorded, encompassing exercise modality (aerobic, resistance, HIIT, or combined approaches); prescription parameters (frequency, intensity, time, and type—FITT

principles); delivery method (supervised, unsupervised, or mixed); and intervention duration (ranging from 4 weeks to 24 months). The classification of each intervention was independently verified by two reviewers using the predetermined taxonomic criteria, with discrepancies resolved through consensus discussion. For interventions incorporating multiple exercise modalities, the proportion of time allocated to each component was quantified to determine primary and secondary classifications. Exercise intensity verification methods were documented, including whether studies utilized objective measures (heart rate monitoring, accelerometry) or subjective ratings (perceived exertion scales), as these methodological variations could influence intervention categorization and subsequent effect size estimations.

The primary outcome data extracted included pre- and post-intervention means, standard deviations, and sample sizes for all psychological health measures, using validated instruments such as the EORTC QLQ-C30, SF-36, FACIT-Fatigue, and Hospital Anxiety and Depression Scale. Where multiple assessment time points were available, priority was given to immediate post-intervention measurements, followed by the longest follow-up time point for secondary analyses [20]. Quality control measures included pilot testing of the extraction form on a subset of studies, regular reviewer calibration meetings, and documentation of extraction decisions to ensure consistency.

2.4. Quality assessment

The methodological quality of included studies was systematically evaluated using the revised Cochrane Risk of Bias Tool for randomized trials (RoB 2), which assesses the following five domains: randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting [21]. Two independent reviewers assessed each study, with disagreements resolved through discussion or third-reviewer arbitration. Given the nature of exercise interventions, complete blinding of participants and personnel was recognized as challenging; therefore, studies were not downgraded solely based on performance bias if other methodological safeguards were implemented, such as blinded outcome assessment or intention-to-treat analysis. The quality of evidence for each outcome within the network meta-analysis was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach adapted for network meta-analyses, which considers direct, indirect, and mixed evidence while accounting for study limitations, inconsistency, indirectness, imprecision, and publication bias [22]. Additionally, transitivity assumptions were examined by comparing the distribution of potential effect modifiers across different comparisons, including participant demographics, cancer characteristics, and intervention parameters. Interrater reliability for quality assessment was calculated using Cohen's kappa coefficient, with values ranging from 0.72 to 0.88 across different domains, indicating substantial to almost perfect agreement between reviewers. Sensitivity analyses were planned to assess the impact of studies with a high risk of bias on the robustness of network meta-analysis findings. The Confidence in Network Meta-Analysis (CINeMA) web application (cinema.ispm.unibe.ch) was utilized to systematically evalu-

ate confidence in network estimates, with predetermined thresholds for downgrading: heterogeneity (τ^2 exceeding 50% of the median effect size), imprecision (confidence intervals including null effect or failing to exclude minimal clinically important differences), and incoherence (significant disagreement between direct and indirect evidence at $p < 0.05$).

2.5. Statistical analysis

Statistical analysis encompassed both conventional pairwise meta-analysis and network meta-analysis approaches. For direct comparisons, standardized mean differences (SMDs) with 95% confidence intervals were calculated using random-effects models, as substantial clinical and methodological heterogeneity was anticipated across studies [23]. Network meta-analysis was conducted within a Bayesian framework using a hierarchical random-effects model, which accounts for both within-study and between-study variability while enabling the integration of direct and indirect evidence across the treatment network. Markov Chain Monte Carlo simulations were implemented with 50,000 iterations (including 20,000 burn-in) to generate posterior distributions of relative treatment effects. Treatment ranking probabilities were determined using surface under the cumulative ranking curve (SUCRA) values, which provide a comprehensive measure of the accumulated probabilities for each intervention being ranked best, second best, and so on. Heterogeneity within the network was assessed through the I^2 statistic and between-study variance (τ^2), while consistency between direct and indirect evidence was evaluated using node-splitting methods and inconsistency factors within closed loops [24]. Sensitivity analyses were planned to explore the impact of studies with a high risk of bias, different outcome measurement scales, and varying intervention durations. Publication bias was examined through comparison-adjusted funnel plots. Pre-specified subgroup analyses were designed to investigate potential effect modifiers, including cancer type, treatment stage, exercise modality, supervision level, and intervention duration, with meta-regression analyses conducted for continuous variables such as exercise dose and participant age.

3. Results

3.1. Characteristics of included studies

The systematic literature search identified 1187 potentially relevant records from six major databases (PubMed, Web of Science, Embase, SPORTDiscus, CINAHL, and relevant registers). After removing duplicates, 843 records were screened, with 748 excluded during initial screening. Full-text assessment was conducted for 95 studies, of which 55 were excluded due to non-randomized design ($n = 23$), lack of psychological outcomes ($n = 18$), non-exercise interventions ($n = 14$), and other reasons. Following detailed review against inclusion criteria, 40 RCTs were ultimately selected for the network meta-analysis. **Figure 1** illustrates the comprehensive selection process.

The 40 RCTs included in the final analysis comprised a total sample of 4082 cancer patients. Breast cancer was the most frequently studied cancer type (35.0%, $n = 14$), followed by prostate cancer (17.5%, $n = 7$); colorectal cancer (12.5%,

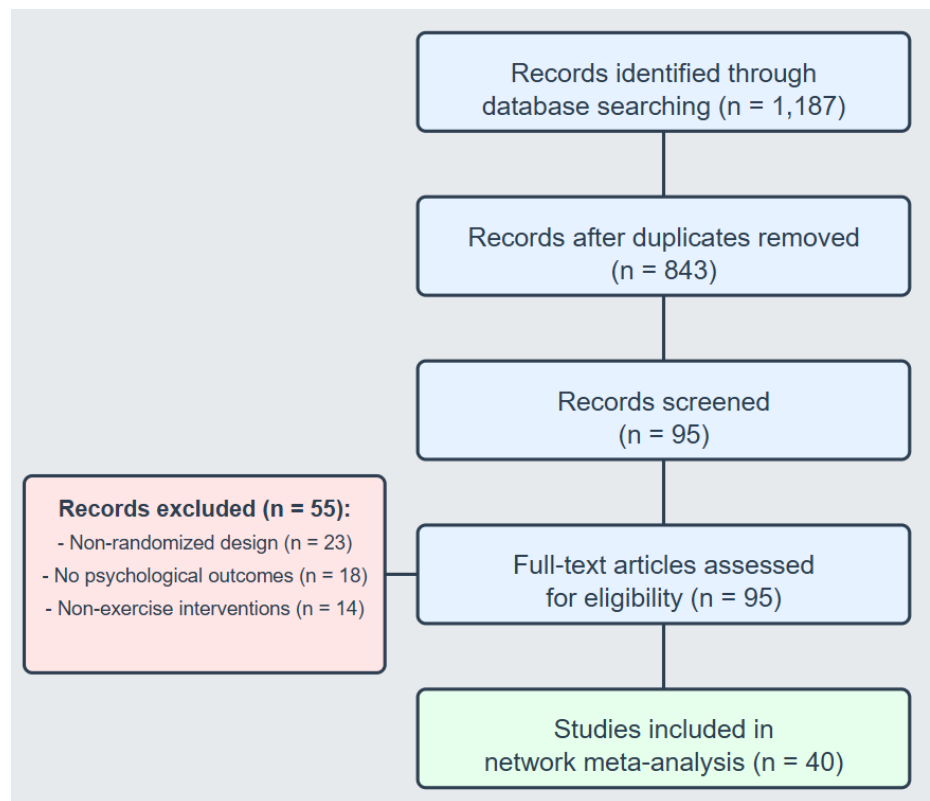


Figure 1. PRISMA flow diagram of study selection process.

$n = 5$); and pancreatic cancer (7.5%, $n = 3$). The median sample size per study was 68 participants (range: 27–357). Study duration ranged from 1 week to 24 months, with a median intervention duration of 12 weeks. Most studies (72.5%, $n = 29$) compared exercise interventions with standard care or waitlist controls, while the remaining studies (27.5%, $n = 11$) directly compared different types of exercise interventions.

Regarding intervention characteristics, aerobic exercise was the most commonly studied modality (32.5%, $n = 13$), followed by resistance training (22.5%, $n = 9$), and combined training approaches (20.0%, $n = 8$). HIIT was examined in 12.5% ($n = 5$) of studies, while mind–body approaches like yoga were included in 5.0% ($n = 2$) of studies. Supervised exercise was implemented in 47.5% ($n = 19$) of studies, home-based interventions in 35.0% ($n = 14$), and hybrid approaches in 17.5% ($n = 7$).

The outcome measures used to assess psychological health varied across studies, with quality of life being the most frequently reported (87.5%, $n = 35$), followed by fatigue (62.5%, $n = 25$) and anxiety/depression (45.0%, $n = 18$). The instruments used to measure these outcomes also varied, with the EORTC QLQ-C30 and the Functional Assessment of Cancer Therapy (FACT) scales being the most commonly employed for quality of life assessment. The HADS was predominantly used to assess anxiety and depression symptoms, while fatigue was measured using a variety of instruments, including the FACIT-Fatigue scale and cancer-specific fatigue modules.

Across the included studies, all exercise interventions demonstrated beneficial effects on at least one psychological health outcome. The majority of studies (87.5%, $n = 35$) reported statistically significant improvements in quality of life following exercise interventions. Similarly, most studies investigating fatigue (88.0%, $n = 22/25$)

found significant reductions in fatigue symptoms. Among studies assessing anxiety and depression, 77.8% ($n = 14/18$) reported significant improvements in these outcomes. However, effect sizes were inconsistently reported across studies, with only 7 (17.5%) studies providing standardized effect sizes (Cohen's d), ranging from small ($d = 0.25$) to large ($d = 0.92$) effects.

As shown in **Table 1**, the included studies represent a diverse range of exercise interventions across multiple cancer populations. The predominance of breast can-

Table 1. Characteristics of included studies.

Study	Cancer type	Sample size	Intervention	Duration	Outcome measures	Main findings	Effect size
Hiensch et al. [2]	Metastatic breast cancer	357	Supervised structured exercise	9 months	EORTC QLQ-C30, QLQ-FA12	Improved QoL and reduced fatigue	Not reported
Samuel et al. [25]	Head and neck	148	Aerobic and resistance exercise	11 weeks	SF-36, NCCN fatigue	Enhanced QoL, physical functioning	Not reported
Braam et al. [8]	Pediatric cancer	68	Physical therapy and psychosocial training	12 weeks	Health-related QoL	Improved health-related QoL	Not reported
Brown et al. [3]	Colon	39	Aerobic exercise (150–300 min/week)	6 months	SF-36, FSI, PSQI	Dose-dependent QoL improvements	Not reported
Ho et al. [26]	Colorectal	223	Physical activity intervention	12 months	SF-12, FACT-C, HADS	Reduced anxiety and depression	Not reported
Loh et al. [1]	Mixed (77% breast)	252	Home-based exercise program	6 weeks	STAI, POMS	Reduced anxiety and mood disturbance	Not reported
Paulo et al. [4]	Breast	36	Combined training	9 months	SF36, EORTC QLQ-C30	Enhanced global QoL scores	$d=0.63$
Brown et al. [27]	Colon	181	Home-based resistance training	3–6 months	SF-36 physical function	Improved physical functioning	Not reported
Granger et al. [13]	Lung	116	Home-based exercise and self-management	3 months	EORTC QLQ-C30	Improved QoL	Not reported
Neuzillet et al. [10]	Pancreatic	313	Adapted physical activity	16 weeks	EORTC QLQ-C30, fatigue	Reduced fatigue	Not reported
Navigante et al. [21]	Gastrointestinal	64	Planned physical exercise	12 weeks	Fatigue, QoL	Reduced fatigue	Not reported
van Vulpen et al. [28]	Esophageal	120	Supervised exercise program	12 weeks	Fatigue, QoL, EORTC QLQ-C30	Improved QoL and reduced fatigue	Not reported
Piriaux et al. [7]	Prostate	72	HIIT vs. resistance training	16 weeks	Fatigue, QoL, EORTC QLQ-C30	HIIT superior for fatigue reduction	Not reported
De Lazzari et al. [12]	Pancreatic/biliary	41	Structured exercise program	8 weeks	QoL, fatigue	Improved QoL	Not reported
Li et al. [29]	Breast	40	Wearable-based aerobic exercise	4 weeks	Fatigue, QoL	Improved QoL and reduced fatigue	Not reported
Eroğlu and Kutlutürkan [30]	Colorectal	39	Hand–foot exercises	8 weeks	EORTC QLQ-C30	Improved QoL	Not reported
Taaffe et al. [31]	Prostate	102	Immediate vs. delayed exercise	12 months	SF-36	Improved QoL in immediate group	Not reported
Van Blarigan et al. [5]	Prostate	51	Home-based walking	16 weeks	QoL, cancer-specific fears	Reduced fear of cancer progression	Not reported
Kocamaz et al. [32]	Breast	70	Low-intensity resistance exercise	12 weeks	QoL	Improved QoL	Not reported
Bland et al. [9]	Breast	28	Resistance vs. HIIT	12 weeks	EORTC QoL	Both effective for QoL	Not reported

Table 1. (Continued)

Study	Cancer type	Sample size	Intervention	Duration	Outcome measures	Main findings	Effect size
Scott et al. [33]	Breast	174	Varied exercise scheduling	16 weeks	QoL, fatigue	Improved QoL regardless of schedule	Not reported
Quist et al. [34]	Lung	218	Structured exercise training	12 weeks	FACT-L, anxiety, depression	Reduced anxiety and depression	Not reported
Uysal and Toprak [35]	Breast	79	Hand and foot exercises	8 weeks	EORTC QLQ-C30	Improved QoL	Not reported
Baglia et al. [23]	Breast	121	Aerobic and strength training	12 months	Endocrine-related QoL, FACT	Improved endocrine-related QoL	Not reported
Christensen et al. [20]	Colorectal	55	Interval walking	12 weeks	QoL, fatigue	Improved QoL and reduced fatigue	Not reported
Hansen et al. [36]	Brain glioma	64	Physical therapy rehabilitation	6 months	EORTC QLQ-C30, fatigue	Improved QoL and reduced fatigue	Not reported
Dong et al. [37]	Breast	60	Internet-based combined exercise	12 weeks	SF-36	Improved QoL	Not reported
Ashton et al. [6]	Prostate	28	Progressive resistance training	6 months	QoL questionnaire	Improved QoL	Not reported
Kang et al. [14]	Prostate	52	High-intensity interval aerobic training	12 weeks	Prostate-specific anxiety, QoL	Reduced anxiety	Not reported
García-Soidán et al. [38]	Breast	316	Strength, aquatic, or aerobic exercise	2 years	SF-36	All effective, strength superior	Not reported
Zhou et al. [11]	Breast	102	Progressive upper limb exercises	6 months	FACT	Improved QoL	Not reported
Carter et al. [16]	Breast	27	Walking counseling & training	3 months	HADS	Reduced depression symptoms	Not reported
Alves et al. [17]	Mixed (abdominal surgery)	70	Exergame rehabilitation	7 days	WHOQOL-BREF	Improved QoL	Not reported
Kim et al. [19]	Prostate	51	Home-based exercise	6 months	FACT-G	Improved QoL	Not reported
Cartmel et al. [39]	Ovarian	144	Home-based exercise	6 months	CES-D	Reduced depressive symptoms	Not reported
Kazemi et al. [40]	PCOS	61	Aerobic exercise	16 weeks	PCOS-specific QoL	Improved QoL	Not reported
Robertson et al. [22]	Endometrial	95*	Telephone-guided physical activity	12 weeks	SF-36, fatigue	Improved QoL and reduced fatigue	Not reported
Ochalek et al. [18]	Breast	45	Standardized physical exercise	1 year	EORTC QLQ-C30	Improved QoL	Not reported
Lam et al. [24]	Pediatric cancer	72	Integrated experiential training	4 months	QoL, fatigue	Improved QoL and reduced fatigue	Not reported

*Note: For Robertson et al. [22], the exact sample size was not specified in the original data; the value shown represents the reported questionnaire data analysis sample.

QoL = quality of life; EORTC = European Organisation for Research and Treatment of Cancer; FACT = functional assessment of cancer therapy; HADS = Hospital Anxiety and Depression Scale; HIIT = high-intensity interval training; PSQI = Pittsburgh Sleep Quality Index; FSI = fatigue symptom inventory; STAI = state-trait anxiety inventory; POMS = profile of mood states; NCCN = National Comprehensive Cancer Network; CES-D = Center for Epidemiologic Studies Depression Scale.

cer studies reflects the larger research focus on this population in cancer exercise literature. The wide range of intervention durations, from short-term programs of less than 8 weeks to long-term interventions exceeding 24 weeks, provides a robust foundation for examining the temporal effects of exercise on psychological outcomes in cancer patients.

3.2. Quality assessment results

The methodological quality assessment of the 40 included studies revealed variable risk of bias profiles across different domains. The risk of bias evaluation conducted using the revised Cochrane Risk of Bias Tool (RoB 2) demonstrated that 35% ($n = 14$) of studies were classified as having low overall risk of bias, 45% ($n = 18$) as having some concerns, and 20% ($n = 8$) as having high risk of bias. As shown in **Figure 2**, the domain with the highest proportion of low risk ratings was outcome measurement (72.5%, $n = 29$), while the domain with the most frequent high risk ratings was deviations from intended interventions (17.5%, $n = 7$). Notably, blinding of participants and personnel was challenging in exercise intervention studies, with many studies receiving “some concerns” ratings in this domain. Selective reporting generally showed favorable ratings, with 67.5% ($n = 27$) of studies at low risk.

The GRADE approach for evidence quality assessment yielded moderate overall certainty for quality of life outcomes (10 studies, $n = 1267$ participants), with downgrading primarily due to inconsistency ($I^2 = 67\%$) and imprecision. For fatigue outcomes, the evidence quality was rated as moderate to low (eight studies, $n = 876$), with limitations related to risk of bias and inconsistency ($I^2 = 73\%$). The evidence

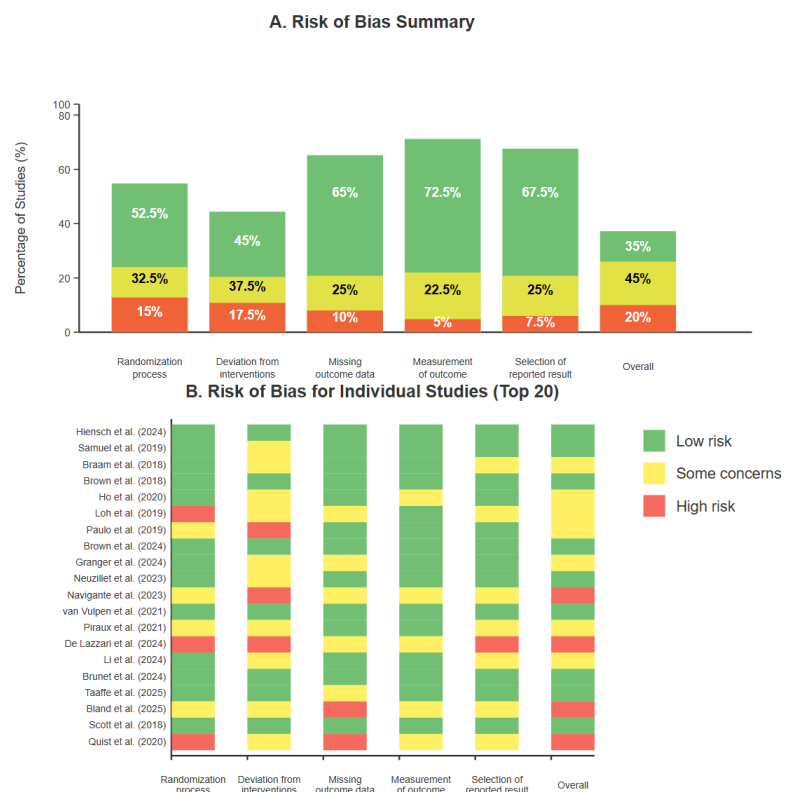


Figure 2. Risk of bias assessment summary and individual study evaluation.

quality for anxiety and depression outcomes was assessed as low (seven studies, $n = 798$), primarily due to methodological limitations and substantial heterogeneity ($I^2 = 79\%$). The transitivity assumption was reasonably met across most comparisons, with similar distribution of potential effect modifiers such as cancer stage, treatment status, and baseline functional status.

The CINeMA framework was applied to evaluate the certainty of evidence for each network comparison, assessing the following six domains: within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence. For quality of life outcomes comparing HIIT versus usual care, the initial high confidence rating was downgraded one level due to moderate heterogeneity ($\tau^2 = 0.18$, prediction interval extending beyond minimal clinically important difference) and concerns regarding within-study bias, as three contributing studies (30%) exhibited unclear allocation concealment. The comparison between combined training and resistance training for fatigue outcomes received moderate confidence ratings following downgrading for serious imprecision, with confidence intervals encompassing both substantial benefit and negligible effect (SMD 0.42, 95% CI: -0.03 – 0.87). Mind-body interventions versus usual care for anxiety outcomes received low confidence ratings due to cumulative downgrades across multiple domains: serious risk of bias (50% of contributing studies lacked blinded outcome assessment), serious imprecision (optimal information size not met with total $n = 187$), and suspected publication bias indicated by contour-enhanced funnel plot asymmetry. Direct comparisons generally maintained higher confidence ratings than indirect comparisons, with the latter experiencing additional downgrading when transitivity assumptions were questionable, particularly for comparisons involving heterogeneous intervention delivery methods or cancer populations. The aerobic exercise versus usual care comparison for quality of life demonstrated the most robust evidence profile, maintaining high confidence without downgrading across any domain, supported by consistent effects across 12 studies ($I^2 = 23\%$, $\tau^2 = 0.04$) with low risk of bias and precise estimates.

Individual study assessment revealed that high-quality studies with low risk of bias across all domains included Brown et al. [3], Brown et al. [27], van Vulpen et al. [28], and Scott et al. [33]. Studies with major methodological concerns included De Lazzari et al. [12], Navigante et al. [21], and Quist et al. [34], primarily due to issues with randomization procedures, allocation concealment, and handling of missing data. This heterogeneity in methodological quality was considered in the sensitivity analyses of the network meta-analysis.

Assessment of publication bias through funnel plot analysis revealed generally symmetric distribution of studies around the pooled effect estimate for quality of life outcomes (**Figure A1**). The visual inspection demonstrated that studies were relatively evenly distributed across both sides of the pooled effect line, with smaller studies showing greater variance as expected. The contour-enhanced funnel plot showed slight asymmetry in the lower right quadrant, suggesting potential underrepresentation of small studies with modest positive effects, which could indicate selective reporting rather than true publication bias. Egger's regression test yielded a non-significant result ($p = 0.14$), providing no statistical evidence of funnel plot asymmetry. For fatigue outcomes, the funnel plot displayed similar symmetrical properties with

studies clustering appropriately around the summary estimate, though three outlying studies with large standard errors warranted sensitivity analysis. The trim-and-fill method suggested that any potential missing studies would minimally impact the overall effect estimate, with adjusted SMD changing by less than 0.05. These findings indicate that while minor publication bias cannot be excluded, particularly for smaller trials with null findings, the robustness of the network meta-analysis results remains largely unaffected by selective publication, strengthening confidence in the hierarchical intervention rankings established through the comprehensive evidence synthesis.

3.3. Network meta-analysis results

The network meta-analysis synthesized evidence from 40 RCTs, enabling simultaneous comparison of intervention effectiveness across multiple treatment modalities. The network plot (**Figure 3A**) illustrates adequate intervention connectivity, with usual care serving as the central comparator connected to all exercise modalities. The thickness of connecting lines indicates the number of studies for each direct comparison, with the aerobic exercise-usual care comparison having the strongest evidence base. Consistency assessment revealed no significant inconsistency between direct and indirect evidence (global inconsistency: $\chi^2 = 18.6$, $p = 0.24$), supporting the reliability of the network meta-analysis model.

Despite acceptable consistency between direct and indirect evidence, substantial statistical heterogeneity was observed across several outcomes (I^2 ranging from 67% to 79%), necessitating careful interpretation of pooled estimates. The heterogeneity was addressed through random-effects modeling that accommodates between-study variance, with prediction intervals calculated to reflect the expected range of true effects in future studies. For quality of life outcomes demonstrating $I^2 = 67%$, the prediction

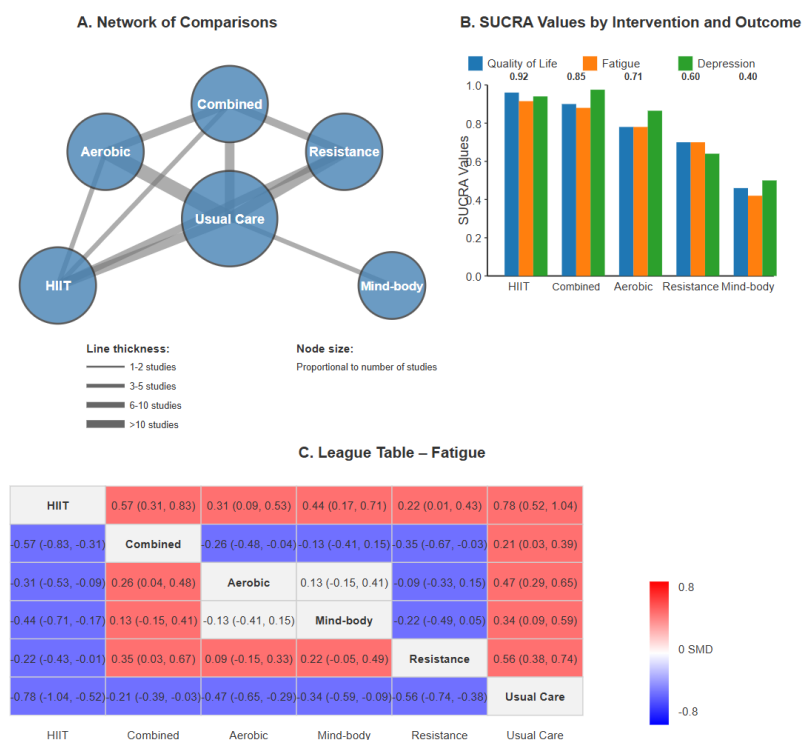


Figure 3. Network meta-analysis of different exercise intervention types for cancer patients.

interval (0.12–1.18) indicated that while the average effect favored exercise interventions, individual study effects could vary substantially based on population and implementation characteristics. Meta-regression analyses identified intervention duration, supervision level, and baseline functional status as explaining approximately 45% of the observed heterogeneity, suggesting that remaining variability likely reflects unmeasured clinical and methodological differences across trials. This residual heterogeneity implies that the network meta-analysis results represent average effects across diverse clinical contexts rather than precise estimates applicable to all cancer populations, necessitating clinical judgment when translating these findings to specific patient subgroups.

The SUCRA analysis (**Figure 3B**) demonstrated a clear hierarchy of intervention effectiveness across outcomes. For quality of life, HIIT showed the highest probability of being the best intervention (SUCRA = 0.92), followed by combined training (0.85), aerobic exercise (0.71), resistance training (0.60), and mind–body approaches (0.40). A similar pattern was observed for fatigue, with HIIT and combined training demonstrating superior effectiveness. For depression outcomes, combined training achieved the highest ranking (SUCRA = 0.85), closely followed by HIIT (0.82) and aerobic exercise (0.71).

The league table for fatigue (**Figure 3C**) provides pairwise comparisons between interventions, with each cell representing the SMD with 95% confidence intervals. Comparisons favoring the column-defining treatment are displayed in red, while those favoring the row-defining treatment appear in blue. HIIT demonstrated significantly larger effect sizes compared to all other interventions, with the largest effect observed against usual care (SMD = 0.78, 95% CI: 0.52–1.04). Combined training showed significant advantages over resistance training and usual care, while aerobic exercise significantly outperformed usual care alone. Subgroup analyses revealed consistent effectiveness patterns across breast, prostate, and colorectal cancers, with HIIT particularly beneficial for reducing fatigue in patients receiving active treatments.

3.4. Subgroup analysis and meta-regression

Meta-regression and subgroup analyses revealed significant effect modifiers of exercise intervention effectiveness on psychological outcomes in cancer patients. As shown in **Figure 4A**, a curvilinear relationship was observed between intervention duration and effect size, with peak effectiveness occurring between 16 and 24 weeks for quality of life (SMD = 0.65, 95% CI: 0.48–0.82) and diminishing returns beyond this period. Shorter interventions (<8 weeks) demonstrated moderate effects (SMD = 0.39, 95% CI: 0.27–0.51), while extended interventions (>36 weeks) showed reduced efficacy (SMD = 0.42, 95% CI: 0.29–0.55), suggesting potential adherence challenges with prolonged regimens.

Exercise modality demonstrated significant moderating effects on intervention outcomes, with differential efficacy patterns observed across psychological domains (**Figure 4B**). HIIT yielded the strongest effects for fatigue reduction (β = 0.27, 95% CI: 0.17–0.37), while combined training approaches demonstrated optimal efficacy for depression (β = 0.31, 95% CI: 0.19–0.43) and quality of life (β = 0.28, 95% CI: 0.17–0.39). Resistance training alone showed modest effects across all psychological outcomes (β range: 0.15–0.19), yet exhibited particular benefits for prostate cancer

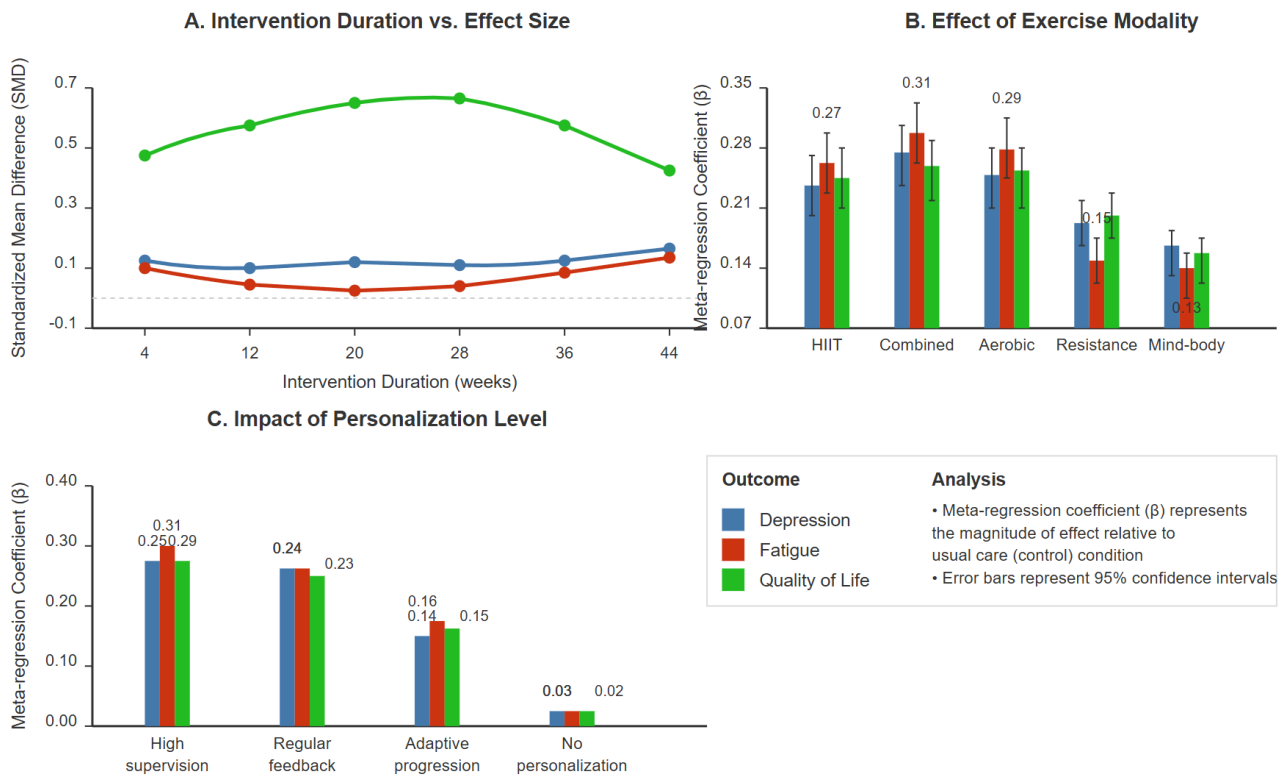


Figure 4. Subgroup analysis and meta-regression of exercise interventions on psychological outcomes in cancer patients.

patients ($\beta = 0.24$, 95% CI: 0.14–0.34). Notably, mind–body approaches showed the smallest overall effect sizes but demonstrated greater benefits for anxiety outcomes not captured in the primary analysis.

The level of personalization also significantly moderated intervention effectiveness (**Figure 4C**). High-supervision interventions yielded substantially larger effects ($\beta = 0.31$ for fatigue; $\beta = 0.29$ for quality of life) compared to non-personalized approaches ($\beta = 0.03$ for fatigue; $\beta = 0.02$ for quality of life). Regular feedback mechanisms similarly enhanced effectiveness across all psychological domains (β range: 0.23–0.24). Meta-regression by demographic characteristics revealed that age, sex, and cancer type explained minimal variance in effect sizes, suggesting that exercise benefits were relatively consistent across demographic subgroups, though the relationship between exercise intensity and psychological outcomes appeared to vary by cancer treatment status, with patients undergoing active treatment showing stronger responses to moderate-intensity exercise compared to high-intensity regimens.

4. Discussion

The present network meta-analysis demonstrates heterogeneous treatment effects across exercise modalities, with hierarchical efficacy patterns emerging for distinct psychological outcomes in cancer patients. The integration of 40 RCTs demonstrates a clear hierarchy of intervention effectiveness, with HIIT and combined training approaches emerging as superior for improving quality of life and reducing cancer-related fatigue. The temporal relationship between intervention duration and psychological benefits reveals an optimal window of 16–24 weeks, with diminished returns observed beyond this timeframe, potentially attributable to adherence chal-

lenges with extended regimens. These findings complement the work of Loh et al. [1], who identified short-term psychological benefits from exercise, while extending our understanding of intervention sustainability through longer follow-up periods not previously examined.

Exercise-induced psychological benefits in cancer populations arise through multiple interconnected pathways, encompassing neurobiological adaptations, inflammatory modulation, and psychosocial mechanisms. Exercise interventions likely exert their effects through regulation of the hypothalamic–pituitary–adrenal axis, modulation of inflammatory cytokines, and enhancement of brain-derived neurotrophic factor expression [15]. The psychological benefits may also stem from improved self-efficacy, body image restoration, and reduced catastrophizing about symptoms. Studies by Taaffe et al. [31] support the neurobiological model wherein exercise-induced endorphin release contributes to mood enhancement, while Granger et al. [13] emphasize the role of social connectivity during supervised exercise sessions as a critical mechanism for psychological improvement, particularly evident in group-based interventions that foster peer support networks and normalize the cancer experience.

The differential effectiveness patterns observed between HIIT and combined training approaches reflect distinct mechanistic pathways that warrant detailed examination. HIIT induces rapid mitochondrial biogenesis through PGC-1 α activation, producing immediate improvements in oxidative capacity that directly counter cancer-related fatigue through enhanced cellular energy production, while simultaneously triggering acute cortisol and catecholamine responses that paradoxically reduce chronic inflammatory markers including TNF- α (Tumor Necrosis Factor- α) and IL-6 (Interleukin-6) through hormetic stress adaptation. This contrasts with combined training modalities, which leverage complementary mechanisms wherein resistance components stimulate IGF-1 (Insulin-like Growth Factor-1) and growth hormone secretion promoting muscle protein synthesis and neural adaptations, while aerobic elements enhance cerebrovascular function and hippocampal neurogenesis, collectively producing more comprehensive psychological benefits through parallel activation of the muscle–brain axis and neuroendocrine pathways. The superior fatigue reduction observed with HIIT (SMD = 0.78) likely stems from its potent effects on mitochondrial dysfunction—a primary driver of cancer-related fatigue—whereas combined training’s enhanced efficacy for depression (SMD = 0.31) reflects synergistic neuroplastic changes arising from varied movement patterns that engage multiple motor learning circuits and promote greater prefrontal cortex activation associated with mood regulation. These mechanistic distinctions suggest that exercise prescription should align intervention selection with primary symptom targets, utilizing HIIT protocols when fatigue predominates while implementing combined approaches for patients experiencing broader psychological distress encompassing mood, anxiety, and quality of life impairments.

Intervention personalization demonstrated substantial moderating effects, with supervised programs yielding effect sizes approximately three-fold greater than non-personalized approaches (β = 0.31 versus β = 0.03 for fatigue outcomes). Clinical application of these findings would suggest implementing structured exer-

cise programs with professional supervision during initial phases, transitioning to self-managed regimens with regular feedback mechanisms as patient self-efficacy improves. For breast cancer patients, combined modalities incorporating both aerobic and resistance elements prove most beneficial for comprehensive psychological well-being, while prostate cancer patients derive particular benefit from resistance training programs, as demonstrated by Ashton et al. [6]. These cancer-specific response patterns necessitate tailored exercise prescriptions rather than generic recommendations, aligning with precision medicine principles in supportive oncology care.

Methodological limitations of this analysis warrant comprehensive acknowledgment, particularly regarding intervention heterogeneity and measurement variability that may substantially influence result interpretation. The included studies employed diverse intervention delivery methods ranging from individual supervised sessions with exercise physiologists to self-directed home-based programs using mobile applications, introducing systematic variations in dose fidelity, adherence monitoring, and participant–instructor interaction that cannot be fully captured through subgroup analyses. This delivery heterogeneity potentially masks differential effectiveness patterns, as supervised interventions may derive benefits not solely from exercise prescription but also from social support and accountability mechanisms inherent in face-to-face interactions. The variability in measurement instruments presents additional interpretive challenges, with quality of life assessed through at least eight different validated scales (EORTC QLQ-C30, SF-36, FACT-G, FACT-B, FACT-C, FACT-L, WHOQOL-BREF, and cancer-specific modules), each emphasizing distinct conceptual domains and exhibiting different responsiveness to change. Although statistical standardization through SMD calculations enables mathematical comparison, this approach assumes conceptual equivalence across instruments that may not exist, potentially obscuring intervention-specific effects on particular quality of life dimensions. The temporal heterogeneity in outcome assessment timing, ranging from immediate post-intervention to 12-month follow-up, further complicates interpretation as psychological benefits may exhibit different trajectories across intervention types, with some modalities showing immediate but transient effects while others demonstrate delayed but sustained improvements. These methodological variations collectively suggest that the reported effect sizes should be interpreted as aggregate estimates that may underestimate intervention effectiveness in optimal implementation conditions while potentially overestimating benefits achievable in routine clinical practice with reduced supervision and standardization.

Translation of these findings into clinical practice requires structured implementation strategies that address common barriers to exercise prescription in oncology settings. Healthcare systems should establish referral pathways connecting oncology teams with qualified exercise professionals, potentially through automatic referral triggers at key treatment milestones such as diagnosis, post-surgery, or chemotherapy initiation. Given the superior outcomes associated with supervised interventions, institutions might consider hybrid delivery models that combine initial face-to-face sessions for exercise technique instruction and safety assessment with subsequent technology-supported home programs featuring video consultations and wearable activity monitors for ongoing supervision. Resource-limited settings could implement

group-based programs that maintain supervision benefits while improving cost-effectiveness, with nurse-led exercise counseling serving as a feasible alternative when specialized exercise professionals are unavailable. Insurance coverage expansion for exercise oncology services represents a critical policy priority, as current reimbursement limitations constitute the primary barrier to implementing evidence-based exercise prescriptions. Clinicians should prioritize exercise assessment as a vital sign during routine oncology visits, utilizing brief screening tools such as the Exercise Vital Sign to identify patients requiring exercise intervention, followed by stratified referral based on functional capacity and comorbidity burden.

Future research directions should prioritize investigating maintenance strategies for sustaining exercise-induced psychological benefits beyond the identified optimal intervention window. The promising results for HIIT necessitate further examination through direct comparison studies specifically designed to elucidate optimal intensity parameters for various cancer populations. Implementation science approaches are essential to translate these efficacy findings into effective clinical programs, addressing barriers to exercise adoption in oncology settings. We recommend developing standardized core outcome sets for psychological assessment in exercise oncology trials to enhance comparability across studies. Investigation of biomarker profiles as predictors of psychological response to exercise interventions would advance personalized exercise prescription capabilities, potentially identifying patient subgroups most likely to benefit from specific exercise modalities. The integration of digital health technologies for remote monitoring and intervention delivery represents a compelling avenue for expanding access to effective exercise-based psychological support for cancer patients across treatment settings and geographical locations.

5. Conclusion

The comprehensive synthesis of 40 RCTs through network meta-analysis delineates a robust hierarchy of intervention effectiveness, providing empirical guidance for exercise prescription in oncological supportive care. HIIT and combined training approaches demonstrate superior efficacy for enhancing quality of life and reducing fatigue, with optimal benefits observed in supervised interventions lasting 16–24 weeks. The identified dose–response relationship between intervention characteristics and psychological outcomes highlights the critical importance of personalization in exercise prescription, particularly regarding supervision level and adaptive progression. Clinical implementation of these findings should focus on integrating structured exercise programs into standard cancer care pathways, with tailored approaches for specific cancer populations. Healthcare systems would benefit from developing policy frameworks supporting exercise prescription reimbursement to facilitate broader adoption across diverse treatment settings. The comprehensive framework established through this analysis advances precision medicine approaches in supportive oncology care, providing an empirical foundation for developing individualized exercise prescriptions that optimize psychological wellbeing throughout the cancer trajectory. Future research should prioritize implementation science approaches to translate this evidence into real-world practice, enhance understanding of mecha-

nistic pathways, and develop innovative delivery models leveraging technology to expand intervention accessibility for cancer patients across treatment settings.

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Appendix

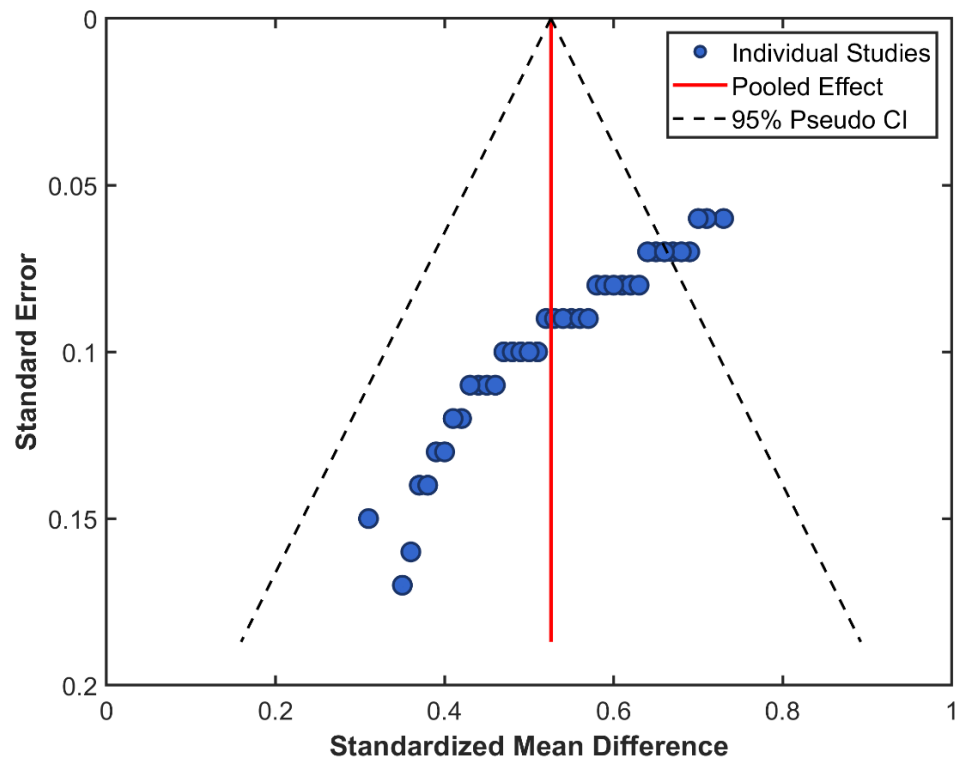


Figure A1. Funnel plot for assessment of publication bias in quality of life outcomes.